Oncologic Applications of Photodynamic Therapy, Including Barrett Esophagus

(80106)

<table>
<thead>
<tr>
<th>Medical Benefit</th>
<th>Effective Date: 08/30/04</th>
<th>Next Review Date: 05/18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preauthorization</td>
<td>No</td>
<td>Review Dates: 09/07, 09/08, 09/09, 05/10, 05/11, 05/12, 05/13, 05/14, 05/15, 05/16, 05/17</td>
</tr>
</tbody>
</table>

**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.

**Description**

Photodynamic therapy (PDT), also called phototherapy, photoradiotherapy, photosensitizing therapy, or phototherapy, 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. Treatment selectivity for tumor cells occurs through selective retention of photosensitizing agent and selective delivery of light.

**Summary of Evidence**

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 a 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 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 radiotherapy. PDT also may be considered for treatment of high-grade dysplasia (HGD) in Barrett esophagus, as controlled and uncontrolled studies have demonstrated favorable complete response rates with the use of PDT. However, radiofrequency ablation and endoscopic mucosal resection appear to be replacing PDT as preferred methods of ablation for HGD in Barrett esophagus.

Data on use of PDT for other malignancies and Barrett esophagus without HGD are limited. The published literature generally comprises small case series without comparator groups. 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 with alternative treatments such as chemoradiation. Thus, the use of PDT for other malignancies and Barrett esophagus without HGD is considered investigational because the impact on health outcomes is unknown.
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 esophagus.

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

Background

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

Barrett Esophagus

The esophagus normally is lined by squamous epithelium. Barrett esophagus is a condition in which 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. Barrett esophagus occurs in the distal esophagus, may involve any length of esophagus, may be focal or circumferential, and is visualized on endoscopy with a different color than background squamous mucosa. Confirmation of Barrett 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 esophagus are at a 40-fold increased risk for developing this disease compared with the general population. Esophageal adenocarcinoma is thought to result from a stepwise accumulation of genetic abnormalities in the specialized epithelium, resulting in histologic phenotypic expression ranging from low-grade dysplasia to HGD to carcinoma. Most patients with nondysplastic Barrett esophagus do not progress beyond nondysplasia; the estimated rate of progression is 0.9% per patient per year. In comparison, the rate of progression from low-grade dysplasia to either HGD or esophageal adenocarcinoma ranges from 0.5% to 13.4% per patient per year. Once HGD is present, the risk of developing adenocarcinoma is 2% to 10% per patient per year; approximately 40% of patients with HGD on biopsy are found to have associated carcinoma in the resection specimen.

Photodynamic Therapy

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 four to six 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 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

Labelled indications for porfimer sodium (FDA-approved in June 2011) are as follows.3

**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 Nd:YAG laser therapy

**Endobronchial Cancer**
- 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

**HGD in Barrett Esophagus**
- Treatment of HGD in Barrett esophagus patients who do not undergo esophagectomy

As of February 2015, oral 5-ALA has not received FDA approval for any indication. Topical 5-ALA used for treatment of actinic keratoses is addressed in a separate protocol (Dermatologic Applications of Photodynamic Therapy).

This protocol addresses only the nondermatologic 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 in a separate protocol.

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 Protocol criteria and are considered investigational. For explanation of experimental and investigational, please refer to the Technology Assessment 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.
References

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


