Corporate Medical Policy

Oncologic Applications of Photodynamic Therapy, Including Barrett's Esophagus

File Name: oncologic_applications_of_photodynamic_therapy_including_barretts_esophagus
Origination: 10/2019
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Description of Procedure or Service

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 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 the photosensitizing agent and selective delivery of light.

PDT has been investigated for use in a wide variety of tumors, including esophageal cancer, cholangiocarcinoma, prostate, bladder, lung, breast, brain (administered intraoperatively), skin, and head and neck cancers. Barrett's esophagus has also 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 (5-ALA), administered orally 4 to 6 hours before the procedure. Aminolevulinic acid (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's 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'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.

Labeled indications for porfimer sodium (Photofrin®), as approved by the U.S. Food and Drug Administration (FDA), 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 neodymium-doped yttrium aluminum garnet 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 patients who do not undergo esophagectomy.

As of May 2023, oral 5-ALA has not yet received FDA approval for as a photosensitizing agent for PDT. Topical 5-ALA, used for the treatment of actinic keratoses, is addressed in a separate policy.

Oncologic Applications of Photodynamic Therapy, Including Barrett's Esophagus

This policy 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 in a separate policy.

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 non-dysplasia. Nondysplastic Barrett's esophagus progresses to high-grade dysplasia at a rate of 0.9% per patient, per year. Progression of low-grade to high-grade dysplasia has been reported as 6–28%. 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.

Related policies:
Dermatologic Applications of Photodynamic Therapy
Focal Treatments for Prostate Cancer

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

BCBSNC will provide coverage for oncologic applications of photodynamic therapy, including Barrett's esophagus when it is determined to be medically necessary because the medical criteria and guidelines noted below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

Oncologic Applications of Photodynamic Therapy, Including Barrett's Esophagus

When Oncologic Applications of Photodynamic Therapy, Including Barrett's Esophagus are covered

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's esophagus;
- palliative treatment of unresectable cholangiocarcinoma when used with stenting.

***Note: Palliative radiation is preferable to photodynamic therapy if feasible for obstructing esophageal and endobronchial lesions.

When Oncologic Applications of Photodynamic Therapy, Including Barrett's Esophagus are not covered

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

Policy Guidelines

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. 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,

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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~~'s~~ 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's 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 (eg, 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.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *96570, 96571, J9600*

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

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Scientific Background and Reference Sources

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Medical Director review 9/2019

Specialty Matched Consultant Advisory Panel 3/2020

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Specialty Matched Consultant Advisory Panel 3/2024

Medical Director review 3/2024

Policy Implementation/Update Information

10/1/19 New policy developed. 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's esophagus, and palliative treatment of unresectable cholangiocarcinoma when used with stenting. Added codes 96570, 96571, and J9600 to Billing/Coding section. References added. Medical Director review 9/2019. **Notification given 10/1/2019 for effective date 1/1/2020**. (krc)

4/14/20 Specialty Matched Consultant Advisory Panel review 3/18/2020. No change to policy statements. (krc)

4/6/21 Specialty Matched Consultant Advisory Panel review 3/17/2021. Reference added. No change to policy statement. (lpr)

4/19/22 Specialty Matched Consultant Advisory Panel review 3/16/2022. Reference added. No change to policy statement. (lpr)

3/31/23 Specialty Matched Consultant Advisory Panel review 3/15/2023. References added. No change to policy statement. (lpr)

4/1/24 Specialty Matched Consultant Advisory Panel review 3/20/2024. References added. No change to policy statement. (lpr)

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Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.