MASSACHUSETTS

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Medical Policy

Oncologic Applications of Photodynamic Therapy, Including Barrett Esophagus

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Policy Number: 454

BCBSA Reference Number: 8.01.06
NCD/LCD: NA

Related Policies

- Dermatologic Applications of Photodynamic Therapy, #463
- Endoscopic Radiofrequency Ablation or Cryoablation for Treatment of Barrett's Esophagus, #218
- Photodynamic Therapy for Choroidal Neovascularization, #600
- Focal Treatments for Prostate Cancer, #733

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

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
- 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.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** for all products if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for products where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is **not required**.
Commercial PPO and Indemnity	Prior authorization is **not required**.
Medicare HMO Blue℠	Prior authorization is **not required**.
Medicare PPO Blue℠	Prior authorization is **not required**.

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:

CPT Codes

CPT codes:	Code Description
31641	Bronchoscopy, rigid or flexible, including fluoroscopic guidance, when performed; with destruction of tumor or relief of stenosis by any method other than excision (eg, laser therapy, cryotherapy)
43229	Esophagoscopy, flexible, transoral; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)
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)
96571	Photodynamic therapy by endoscopic application of light to ablate abnormal tissue via activation of photosensitive drug(s); each additional 15 minutes

HCPCS Codes

HCPCS codes:	Code Description
J9600	Porfimer sodium, 75 mg

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT and HCPCS codes above if medical necessity criteria are met:

ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
C15.3	Malignant neoplasm of upper third of esophagus
C15.4	Malignant neoplasm of middle third of esophagus
C15.5	Malignant neoplasm of lower third of esophagus
C15.8	Malignant neoplasm of overlapping sites of esophagus

C15.9	Malignant neoplasm of esophagus, unspecified
C22.1	Intrahepatic bile duct carcinoma
C24.0	Malignant neoplasm of extrahepatic bile duct
C24.1	Malignant neoplasm of ampulla of Vater
C24.8	Malignant neoplasm of overlapping sites of biliary tract
C24.9	Malignant neoplasm of biliary tract, unspecified
C34.00	Malignant neoplasm of unspecified main bronchus
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.10	Malignant neoplasm of upper lobe, unspecified bronchus or lung
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.30	Malignant neoplasm of lower lobe, unspecified bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.80	Malignant neoplasm of overlapping sites of unspecified bronchus and lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C34.90	Malignant neoplasm of unspecified part of unspecified bronchus or lung
C34.91	Malignant neoplasm of unspecified part of right bronchus or lung
C34.92	Malignant neoplasm of unspecified part of left bronchus or lung
C78.00	Secondary malignant neoplasm of unspecified lung
C78.01	Secondary malignant neoplasm of right lung
C78.02	Secondary malignant neoplasm of left lung
C78.7	Secondary malignant neoplasm of liver and intrahepatic bile duct
C78.80	Secondary malignant neoplasm of unspecified digestive organ
C78.89	Secondary malignant neoplasm of other digestive organs
D00.1	Carcinoma in situ of esophagus
D02.20	Carcinoma in situ of unspecified bronchus and lung
D02.21	Carcinoma in situ of right bronchus and lung
D02.22	Carcinoma in situ of left bronchus and lung
K22.711	Barrett's esophagus with high grade dysplasia

Description

OBSTRUCTING TUMORS

Esophageal cancer is usually diagnosed at an advanced stage. A common clinical manifestation is dysphagia caused by obstruction of the esophagus by the tumor. Lung cancer is a common cause of airway obstruction that can manifest as dyspnea, coughing, and wheezing. The intervention used to manage obstruction depends on several factors, including etiology and acuteness.

Treatment

There are several nonsurgical approaches to provide palliation of dysphagia including photodynamic therapy (PDT). For patients without life-threatening airway obstruction, PDT is an option for providing palliative relief of symptoms.

EARLY-STAGE LUNG CANCER

Less than one-third of lung cancer patients present with early-stage disease. It is anticipated that relatively few patients with nonobstructing lung cancer (who are not candidates for surgery) 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 radiotherapy. Candidates for PDT are limited to those patients who cannot tolerate surgery or radiotherapy, most commonly due to underlying emphysema, other respiratory disease, or prior radiotherapy.

Treatment
For patients with early-stage disease, surgery is the standard treatment. For inoperable early non-small-cell lung cancer (v.4.2018), treatment guidelines from the National Comprehensive Cancer Network recommend stereotactic ablative radiotherapy. The guidelines reference a phase 2 multicenter noncomparative trial of stereotactic body radiotherapy by Baumann et al (2009) who assessed 57 patients with inoperable stage I non-small-cell lung cancer, the results of which demonstrated a 3-year overall survival of 88%. For patients who are not surgical candidates or who refuse surgery and are ineligible for radiotherapy, other ablative techniques (eg, PDT) are options.

BARRETT ESOPHAGUS
The esophagus is normally 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; it may involve any length of the esophagus, it may be focal or circumferential, and it 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 high-grade dysplasia (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. By 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.

Treatment
Management of Barrett esophagus includes endoscopic surveillance, in order to detect the development of dysplasia or esophageal adenocarcinoma as early as possible to provide effective treatment. If low-grade dysplasia is detected, continued surveillance, radiofrequency ablation, or other endoscopic eradication therapies may be recommended. For patients with HGD, endoscopic eradication therapies are recommended, with the type of procedure dependent on patient age and life expectancy, comorbidities, the extent of dysplasia, local expertise in surgery and endoscopy, and patient preference.

CHOLANGIOCARCINOMA
Cholangiocarcinoma is rare and the prognosis is generally poor due to the advanced stage at presentation. Patients with unresectable cholangiocarcinoma typically decline rapidly with symptoms of biliary obstruction.

Treatment
Several palliative therapies have been suggested, including PDT, to reduce symptoms and improve quality of life.

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. PDT for focal treatment of prostate cancer is discussed in evidence review/

Several photosensitizing agents have been used in PDT: porfimer sodium (Photofrin), administered intravenously 48 hours before light exposure, and 5-aminolevulinic acid, administered orally 4 to 6 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.

Summary

For individuals who have obstructing esophageal cancer who receive PDT as palliation, the evidence includes systematic reviews, RCTs, and uncontrolled single-arm studies. Relevant outcomes are change in disease status, symptoms, quality of life, and treatment-related morbidity. A meta-analysis comparing PDT with Nd:YAG laser suggested that improvements in dysphagia are similar, although estimates are imprecise. Compared with the Nd:YAG laser, PDT is associated with a lower risk of perforation and a higher risk of adverse reactions to the light (eg, 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 RCTs and uncontrolled single-arm studies. Relevant outcomes are change in disease status, symptoms, quality of life, and treatment-related morbidity. Evidence from RCTs comparing PDT with Nd:YAG 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. Relevant outcomes are overall survival, disease-specific survival, change in disease status, quality of life, 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 (eg, 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 who have Barrett esophagus with high-grade dysplasia who receive PDT, the evidence includes an RCT and observational studies. Relevant outcomes are overall survival, disease-specific survival, change in disease status, quality of life, and treatment-related morbidity. The 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 5 years of follow-up for patients in the PDT group. The results of the RCT also revealed that patients treated with PDT had significantly more complications, including a high rate of strictures. Observational comparative data have suggested similar mortality outcomes for PDT and esophagectomy over 5 years. 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. Relevant outcomes are change in disease status, symptoms, quality of life, 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 overall survival, with similar adverse event rates. Case series have suggested an improvement in quality of life 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. Relevant outcomes are overall survival, disease-specific survival, change in disease status, quality of life, 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 History

Date	Action
9/2018	BCBSA National medical policy review. No changes to policy statements. New references added. Background and summary clarified.
1/2018	BCBSA National medical policy review. New medically necessary indications described. Clarified coding information. Effective 1/1/2018.
5/2015	Added new references from BCBSA National medical policy. Clarified coding language.
7/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
5/2014	New references from BCBSA National medical policy.
1/2014	Added new CPT code 43229 and removed deleted code 43228.
6/2013	New references from BCBSA National medical policy.
5/2013	New references from BCBSA National medical policy.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
10/2011	Reviewed - Medical Policy Group - Gastroenterology, Nutrition and Organ Transplantation. No changes to policy statements.
7/2011	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
4/2011	Reviewed - Medical Policy Group - Cardiology and Pulmonology. No changes to policy statements.
11/2010	Reviewed - Medical Policy Group - Gastroenterology, Nutrition and Organ Transplantation. No changes to policy statements.
9/2010	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
3/2010	Reviewed - Medical Policy Group- Allergy and ENT/Otolaryngology. No changes to policy statements.
11/2009	Reviewed - Medical Policy Group - Gastroenterology, Nutrition and Organ Transplantation. No changes to policy statements.
9/2009	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
3/2009	Reviewed - Medical Policy Group- Allergy and ENT/Otolaryngology. No changes to policy statements.
2/2009	BCBSA National medical policy review. No changes to policy statements.
11/2008	Reviewed - Medical Policy Group - Gastroenterology, Nutrition and Organ Transplantation. No changes to policy statements.
10/2008	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
3/2008	Reviewed - Medical Policy Group - Allergy and ENT/Otolaryngology. No changes to policy statements.
11/2007	Reviewed - Medical Policy Group - Gastroenterology, Nutrition and Organ Transplantation. No changes to policy statements.

11/2007	BCBSA National medical policy review. No changes to policy statements.
9/2007	Reviewed - Medical Policy Group - Hematology and Oncology. No changes to policy statements.
8/2007	BCBSA National medical policy review. No changes to policy statements.
3/2007	Reviewed - Medical Policy Group- Allergy and ENT/Otolaryngology. No changes to policy statements.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

Medical Policy Terms of Use
Managed Care Guidelines
Indemnity/PPO Guidelines
Clinical Exception Process
Medical Technology Assessment Guidelines

References

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