

MEDICAL POLICY

POLICY TITLE	ONCOLOGIC APPLICATIONS OF PHOTODYNAMIC THERAPY INCLUDING BARRETT'S ESOPHAGUS
POLICY NUMBER	MP 4.019

CLINICAL BENEFIT	☐ MINIMIZE SAFETY RISK OR CONCERN. ☐ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☒ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	12/1/2024

[POLICY](#)
[RATIONALE](#)
[DISCLAIMER](#)
[POLICY HISTORY](#)
[PRODUCT VARIATIONS](#)
[DEFINITIONS](#)
[CODING INFORMATION](#)
[DESCRIPTION/BACKGROUND](#)
[BENEFIT VARIATIONS](#)
[REFERENCES](#)

I. 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 individuals 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.

Other oncologic applications of photodynamic therapy including, but not limited to, other malignancies and Barrett's esophagus without associated high-grade dysplasia, are considered **investigational** as there is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

The National Comprehensive Cancer Network (NCCN) is a nonprofit alliance of cancer centers throughout the United States. NCCN develops the Clinical Practice Guidelines in Oncology which are recommendations aimed to help health care professionals diagnose, treat and manage patients with cancer. Guidelines evolve continuously as new treatments and diagnostics emerge and may be used by Capital Blue Cross when determining medical necessity according to this policy.

Cross-references:

MP 1.118 Endoscopic Radiofrequency Ablation or Cryoablation for Barrett's Esophagus

MP 2.068 Extracorporeal Photophoresis

MEDICAL POLICY

POLICY TITLE	ONCOLOGIC APPLICATIONS OF PHOTODYNAMIC THERAPY INCLUDING BARRETT'S ESOPHAGUS
POLICY NUMBER	MP 4.019

MP 4.008 Photodynamic or Photocoagulation Therapy for Choroidal Neovascularization
MP 4.018 Dermatologic Applications of Photodynamic Therapy
MP 4.043 Treatments of the Prostate

II. PRODUCT VARIATIONS

[TOP](#)

This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below.

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

<https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>.

III. DESCRIPTION/BACKGROUND

[TOP](#)

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.

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 4.043

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.

MEDICAL POLICY

POLICY TITLE	ONCOLOGIC APPLICATIONS OF PHOTODYNAMIC THERAPY INCLUDING BARRETT'S ESOPHAGUS
POLICY NUMBER	MP 4.019

Regulatory Status

Labeled indications for porfimer sodium (Photofrin; Pinnacle Biologics), as approved by the U.S. Food and Drug Administration (FDA), are as follows:

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 May 2024, oral 5-aminolevulinic acid has not received FDA approval as a photosensitizing agent for PDT. It is currently only indicated as an adjunct for the visualization of malignant tissue during surgery in individuals with glioma. Topical 5-aminolevulinic acid, used for the treatment of actinic keratoses, is addressed separately (evidence review 4.018).

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.

IV. RATIONALE

[TOP](#)

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. Relevant outcomes are change in disease status, symptoms, quality of life, and treatment-related morbidity. A meta-analysis comparing PDT with neodymium-doped yttrium aluminum garnet (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 (e.g. photosensitivity). PDT plus argon plasma coagulation appears to prolong the time to recurrence of dysphagia as

MEDICAL POLICY

POLICY TITLE	ONCOLOGIC APPLICATIONS OF PHOTODYNAMIC THERAPY INCLUDING BARRETT'S ESOPHAGUS
POLICY NUMBER	MP 4.019

opposed to argon plasma coagulation alone. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have obstructing endobronchial cancer 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 an improvement in the net health outcome.

For individuals who have early-stage non-small-cell lung cancer (NSCLC) 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 (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 an improvement in the net health outcome.

For individuals with Barrett esophagus with high-grade dysplasia who receive PDT, the evidence includes 2 systematic reviews and 2 RCTs. Relevant outcomes are OS, disease-specific survival, change in disease status, quality of life, 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 5 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 an 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. Three 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

MEDICAL POLICY

POLICY TITLE	ONCOLOGIC APPLICATIONS OF PHOTODYNAMIC THERAPY INCLUDING BARRETT'S ESOPHAGUS
POLICY NUMBER	MP 4.019

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 an 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. 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 small case series without comparator groups. The evidence is insufficient to determine that the technology results in an improvement in the net health outcomes.

V. DEFINITIONS

[TOP](#)

N/A

VI. BENEFIT VARIATIONS

[TOP](#)

The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits, and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

VII. DISCLAIMER

[TOP](#)

Capital Blue Cross' medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

MEDICAL POLICY

POLICY TITLE	ONCOLOGIC APPLICATIONS OF PHOTODYNAMIC THERAPY INCLUDING BARRETT'S ESOPHAGUS
POLICY NUMBER	MP 4.019

VIII. CODING INFORMATION

[TOP](#)

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Covered when medically necessary:

Procedure Codes								
31641	43229	96570	96571	J9600				

ICD-10-CM Diagnosis Codes	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
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

MEDICAL POLICY

POLICY TITLE	ONCOLOGIC APPLICATIONS OF PHOTODYNAMIC THERAPY INCLUDING BARRETT'S ESOPHAGUS
POLICY NUMBER	MP 4.019

ICD-10-CM Diagnosis Codes	Description
C78.02	Secondary malignant neoplasm of left lung
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

IX. REFERENCES

[Top](#)

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MEDICAL POLICY

POLICY TITLE	ONCOLOGIC APPLICATIONS OF PHOTODYNAMIC THERAPY INCLUDING BARRETT'S ESOPHAGUS
POLICY NUMBER	MP 4.019

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MEDICAL POLICY

POLICY TITLE	ONCOLOGIC APPLICATIONS OF PHOTODYNAMIC THERAPY INCLUDING BARRETT'S ESOPHAGUS
POLICY NUMBER	MP 4.019

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MEDICAL POLICY

POLICY TITLE	ONCOLOGIC APPLICATIONS OF PHOTODYNAMIC THERAPY INCLUDING BARRETT'S ESOPHAGUS
POLICY NUMBER	MP 4.019

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MEDICAL POLICY

POLICY TITLE	ONCOLOGIC APPLICATIONS OF PHOTODYNAMIC THERAPY INCLUDING BARRETT'S ESOPHAGUS
POLICY NUMBER	MP 4.019

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MEDICAL POLICY

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X. Policy HISTORY

[TOP](#)

MP 4.019	02/14/2020 Consensus Review. Policy updated with literature review; references added. Policy statements unchanged.
	10/04/2021 Consensus Review. No change to policy statement. NCCN statement added. References updated.
	11/21/2022 Consensus Review. No change to policy statement intent, updated for clarity. References, formatting, and coding reviewed and updated.
	06/13/2023 Administrative Update. Added New Code 0398U Effective 7/1/23.
	08/17/2023 Consensus Review. No change to policy statement. Background updated. References reviewed and updated. Coding reviewed.
	01/19/2024 Administrative Update. Clinical benefit added.
	09/11/2024 Consensus Review. No change to policy statement. Cross Referenced policies, Background, Rational and References updated. Removed CPT code 0398U.

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