MEDICAL POLICY

Medical Policy Title	**Photodynamic Therapy for Malignant Disease**
Policy Number	**8.01.06**
Current Effective Date	February 20, 2025
Next Review Date	February 2026

Our medical policies are based on the assessment of evidence based, peer-reviewed literature, and professional guidelines. Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract. (Link to Product Disclaimer)

POLICY STATEMENT(S)

I. Photodynamic therapy (PDT) with Photofrin is considered **medically appropriate** for **ANY** of the following indications:

- A. Treatment of early-stage non-small-cell lung cancer (NSCLC) in patients who are ineligible for surgery and radiation therapy;
- B. Reduction of obstruction and palliation of symptoms in patients with completely or partially obstructing endobronchial lesions;
- C. Palliative treatment of obstructing esophageal cancer;
- D. Treatment of Barrett's high-grade dysplasia (HGD) in patients who:
  1. are considered at high risk for adverse outcomes (morbidity and mortality) during prophylactic esophagectomy surgery; **and**
  2. decide on this treatment method, based on shared decision-making with their physician and understanding the actual risks and benefits of various treatment options;
- E. Palliative treatment of unresectable cholangiocarcinoma as an adjunct to stenting.

II. PDT with 5-aminolevulinic acid (5-ALA) topical preparation is considered **medically appropriate** for **EITHER** of the following indications:

- A. Superficial and nodular basal cell skin cancer, only when surgery and/or radiation is contraindicated;
- B. Bowen's disease (cutaneous squamous cell carcinoma in situ), only when surgery and/or radiation is contraindicated.

III. PDT is considered **investigational** in the treatment of other types of malignancies, including but not limited to colon, rectal, pancreas, hepatocellular, mesothelioma, prostate, bladder, brain, head and neck cancers, soft tissue sarcoma and Barrett's esophagus (other than HGD, as stated above).

IV. PDT with porfimer sodium (Photofrin) is contraindicated in patients with **ANY** of the following:

- A. Known bone marrow suppression;
- B. Porphyria or known allergies to porphyrins;

C. Existing tracheoesophageal or broncho-esophageal fistula;

D. Tumors eroding into a major vessel;

E. Esophageal or gastric varices or esophageal ulcers greater than one (1) cm in diameter.

RELATED POLICIES

Corporate Medical Policy

8.01.01 Extracorporeal Photochemotherapy/Photopheresis

8.01.11 Ocular Photodynamic Therapy

8.01.21 Light and Laser Therapies for Dermatological Conditions

7.01.01 Focal Therapies for Prostate Cancer Treatment

11.01.10 Clinical Trials

11.01.03 Experimental or Investigational Services

POLICY GUIDELINE(S)

I. A second laser treatment (with no additional Photofrin) can be given 96-120 hours after the first injection, preceded by debridement (via endoscopy) 48 hours after the initial light application.

II. Patients may receive a second course of PDT (with Photofrin) a minimum of 30 days after the initial therapy. Up to three (3) courses of PDT (every 30 days) can be given.

III. As pathologists do not always agree on differentiating between low- and high-grade dysplasia and between high-grade dysplasia and carcinoma in situ, in many cases, high-grade Barrett's dysplasia is confirmed by two pathologists with expertise in gastrointestinal pathology.

DESCRIPTION

PDT is a cancer treatment method using intravenous injection of a photosensitizing agent (e.g., porfimer sodium, Photofrin) and exposure of tumor cells to a laser light source to cause cellular damage. The clearance of porfimer sodium occurs over a period of time (40-72 hours) in normal tissue; however, tumor cells retain porfimer for a longer period. Treatment of the tumor is the result of selective retention of porfimer and selective delivery of light.

PDT with Photofrin is a two-stage process. The first stage is the intravenous injection of Photofrin. Illumination with 630-nm wavelength laser light constitutes the second stage of therapy. The laser treatment induces a photochemical, not a thermal, effect. The photochemical reaction results in the release of toxic, singlet oxygen that causes tumor necrosis.

PDT should not be confused with extracorporeal photopheresis, which is the treatment of certain skin malignancies through the use of ultraviolet light irradiation of the patient's blood.

SUPPORTIVE LITERATURE

Published studies have shown that PDT with Photofrin improves the quality of life (e.g., relief of dysphagia, improvement in dyspnea) and relieves obstruction by reducing tumor mass for those patients with obstructing tumors of the esophagus or endobronchial tree. For those patients with microinvasive NSCLC, not amenable to surgery or radiation, who were treated with PDT, reported tumor response rates (50-84%) and disease-free survival rates (2.7-4.1 years) are favorable. Studies investigating the Nd:YAG laser and PDT found that survival rates were comparable, and that PDT was technically easier to perform, more comfortable for patients, and caused fewer side effects (e.g., perforation).

In a systematic review and meta-analysis, investigators examined the effectiveness of PDT in the treatment of Bowen disease (BD) and cutaneous squamous cell carcinoma (cSCC) for clearance rate (CR) after 1 year. A total of 43 studies were included, enrolling 1,943 BD lesions and 282 SCC lesions. Pooled CRs for BD and SCC were 76 % (95 % CI: 71 % to 80%; I2 = 78.9 %) and 51 % (95 % CI: 35 % to 66 %; I2 = 85.7 %), respectively. The authors concluded that these findings supported the selective use of PDT for BD; however, patients should be advised of potential for recurrence. Moreover, these researchers stated that although PDT can be used for certain cases of cSCC, the high rate of treatment failure necessitates close surveillance for residual or recurrent disease; further studies are needed to justify the usage of PDT in the treatment of BD and cSCC (Yongpisarn 2022).

PDT has also been evaluated as an adjunct to stenting and drainage as a palliative treatment for unresectable bile duct cancer. Two pivotal yet small RCTs have demonstrated improvements in survival.

Ortner et al. (2003) conducted a prospective, open-label, randomized multicenter study that aimed to compared PDT in addition to stenting with stenting alone in patients with NCC. A total of 39 patients with non-resectable cholangiocarcinoma were randomized to either PDT plus stenting (Group A, n =20) or stenting alone (Group B, n = 19). Investigators reported that the median survival was 493 days (95% CI, 276–710) in group A and 98 days (95% CI, 87–107) in group B ($P < 0.0001$). The investigators noted that PDT also improved biliary drainage and quality of life.

Zoepf et al. (2005) conducted a randomized controlled study that investigated the influence of PDT on survival time in advanced bile duct cancer (BDC). A total of 32 patients with non-resectable cholangiocarcinoma were randomized. Light activation was performed in the patients assigned to PDT 48 hours after intravenous application of 2 mg/kg body weight of Photosan-3, an oligomer of hematoporphyrin that has been approved for use in the European Union but is not approved by the FDA. In the control group, patients were treated with stenting and drainage without PDT. The investigators stated that the PDT group and the control group were comparable due to age, gender, performance status, bilirubin level, and bile duct cancer stage. The investigators reported that the median survival time after randomization was 7 months for the control group and 21 months for the PDT group ($p = 0.0109$). The investigators noted that, in 50 % of the initially percutaneously treated patients, they were able to change from percutaneous to transpapillary drainage after PDT.

Although PDT (using porfimer sodium or other photosensitizing agents) has been used in treatment of other cancers, all are either in Phase I or Phase II studies and have not yet been proven outside an investigational setting.

PROFESSIONAL GUIDELINE(S)

The 2024 National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology state that in patients with superficial basal cell carcinoma or squamous cell carcinoma in situ, therapies such as topical imiquimod, topical 5-fluorouracil (5-FU), or photodynamic therapy (PDT) may be considered, although cure rates are approximately 10% lower than for surgical treatment modalities. These options are also recommended for patients where surgery or radiation therapy is contraindicated or impractical.

Additionally, the NCCN Clinical Practice Guidelines (V.5.2024) Biliary Tract Cancers states, "Photodynamic therapy (PDT) is an ablative therapy that involves intravenous injection of a photosensitizing drug followed by selective irradiation with light of a specific wavelength to initiate localized drug activation and has been used for palliation in patients with extrahepatic cholangiocarcinoma (CCA). The combination of PDT with biliary stenting was reported to be associated with prolonged overall survival (OS) in patients with unresectable CCA in two small RCTs." (Ortner et al., 2003 and Zoepf et al., 2005).

REGULATORY STATUS

Photofrin (porfimer sodium) is the only photosensitizing agent with specific indications for use that has been approved by the U.S. Food and Drug Administration (FDA). It was approved in 2003.

CODE(S)

- Codes may not be covered under all circumstances.
- Code list may not be all inclusive (AMA and CMS code updates may occur more frequently than policy updates).
- (E/I)=Experimental/Investigational
- (NMN)=Not medically necessary/appropriate

CPT Codes

Code	Description
96570	Photodynamic therapy by endoscopic application of light to ablate abnormal tissue via activation of photosensitive drugs(s); first 30 minutes (List separately in addition to code for endoscopy or bronchoscopy procedures of lung and gastrointestinal tract)
96571	each additional 15 minutes

HCPCS Codes

Code	Description
J9600	Drug; porfimer sodium, 75 mg

ICD10 Codes

Code	Description
C15.3 - C15.9	Malignant neoplasm esophagus (code range)
C34.00 - C34.92	Malignant neoplasm bronchus and lung (code range)
C78.00 - C78.02	Secondary malignant neoplasm of lung (code range)
C78.80 - C78.89	Secondary malignant neoplasm of other and unspecified digestive organs (code range)
D00.1	Carcinoma in situ of esophagus
D02.20 - D02.22	Carcinoma in situ of bronchus and lung (code range)
K22.70 - K22.719	Barrett's esophagus (code range)

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SEARCH TERMS

Blue light therapy

CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS)

Based on our review, photodynamic therapy for malignant conditions is not specifically addressed in National or Regional Medicare coverage determinations or policies.

PRODUCT DISCLAIMER

- Services are contract dependent; if a product does not cover a service, medical policy criteria do not apply.
- If a commercial product (including an Essential Plan or Child Health Plus product) covers a specific service, medical policy criteria apply to the benefit.
- If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.
- If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.
- If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service, please refer to the Medicaid Product coverage line.

POLICY HISTORY/REVISION

Committee Approval Dates

12/20/01, 01/16/03, 01/15/04, 10/20/04, 08/18/05, 06/15/06, 05/17/07, 05/14/08, 06/18/09, 05/27/10, 04/21/11, 04/19/12, 03/21/13, 02/20/14, 02/19/15, 02/18/16, 02/16/17, 02/15/18, 02/21/19, 02/20/20, 02/18/21, 02/17/22, 02/16/23, 02/22/24, 02/20/25

Date	Summary of Changes
02/20/25	• Annual review, policy statement added for PDT as medically appropriate for palliative treatment of unresectable cholangiocarcinoma as an adjunct to stenting.
01/01/25	• Summary of changes tracking implemented.
10/18/01	• Original effective date