

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

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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

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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

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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

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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.

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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

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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

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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

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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

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N/A

VI. BENEFIT VARIATIONS

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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

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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.

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VIII. CODING INFORMATION

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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

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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

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1. Pinnacle Biologics. Photofrin (porfimer sodium) Injection [prescribing information]. 2019
2. Fayter D, Corbett M, Heirs M, et al. A systematic review of photodynamic therapy in the treatment of pre- cancerous skin conditions, Barrett's oesophagus and cancers of the biliary tract, brain, head and neck, lung, oesophagus and skin. *Health Technol Assess.* Jul 2010;14(37):1-288. PMID 20663420
3. Dai Y, Li C, Xie Y, et al. Interventions for dysphagia in oesophageal cancer. *Cochrane Database Syst Rev.* Oct 30 2014;10(10):CD005048. PMID 25354795
4. Lightdale CJ, Heier SK, Marcon NE, et al. Photodynamic therapy with porfimer sodium versus thermal ablation therapy with Nd:YAG laser for palliation of esophageal cancer: a multicenter randomized trial. *Gastrointest Endosc.* Dec 1995;42(6):507-512. PMID 8674919
5. Heier SK, Rothman KA, Heier LM, et al. Photodynamic therapy for obstructing esophageal cancer: light dosimetry and randomized comparison with Nd:YAG laser therapy. *Gastroenterology.* Jul 1995;109(1):63-72. PMID 7541003
6. Rupinski M, Zagorowicz E, Regula J, et al. Randomized comparison of three palliative regimens including brachytherapy, photodynamic therapy, and APC in patients with malignant dysphagia (CONSORT 1a) (Revised II). *Am J Gastroenterol.* Sep 2011;106(9):1612-1620. PMID 21670770
7. McCann P, Stafinski T, Wong C, et al. The safety and effectiveness of endoscopic and non-endoscopic approaches to the management of early esophageal cancer: a systematic review. *Cancer Treat Rev.* Feb 2011;37(1):11-62. PMID 20570442
8. Li LB, Xie JM, Zhang XN, et al. Retrospective study of photodynamic therapy vs photodynamic therapy combined with chemotherapy and chemotherapy alone on advanced esophageal cancer. *Photodiagnosis Photodyn Ther.* Sep 2010;7(3):139-143. PMID 20728836
9. Akopov A, Rusanov A, Gerasin A, et al. Preoperative endobronchial photodynamic therapy improves resectability in initially irresectable (inoperable) locally advanced non-small cell lung cancer. *Photodiagnosis Photodyn Ther.* Sep 2014;11(3):259-264. PMID 24704942

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10. Diaz-Jimenez JP, Martinez-Ballarín JE, Llunell A, et al. Efficacy and safety of photodynamic therapy versus Nd- YAG laser resection in NSCLC with airway obstruction. *Eur Respir J.* Oct 1999;14(4):800-805. PMID 10573224
11. Kato H, Okunaka T, Shimatani H. Photodynamic therapy for early stage bronchogenic carcinoma. *J Clin Laser Med Surg.* Oct 1996;14(5):235-238. PMID 9612188
12. Endo C, Miyamoto A, Sakurada A, et al. Results of long-term follow-up of photodynamic therapy for roentgenographically occult bronchogenic squamous cell carcinoma. *Chest.* Aug 2009;136(2):369-375. PMID 19318660
13. Moghissi K, Dixon K, Thorpe JA, et al. Photodynamic therapy (PDT) in early central lung cancer: a treatment option for patients ineligible for surgical resection. *Thorax.* May 2007;62(5):391-395. PMID 17090572
14. Corti L, Toniolo L, Boso C, et al. Long-term survival of patients treated with photodynamic therapy for carcinoma in situ and early non-small-cell lung carcinoma. *Lasers Surg Med.* Jun 2007;39(5):394-402. PMID 17565719
15. Furukawa K, Kato H, Konaka C, et al. Locally recurrent central-type early stage lung cancer < 1.0 cm in diameter after complete remission by photodynamic therapy. *Chest.* Nov 2005;128(5):3269-3275. PMID 16306036
16. Cortese DA, Edell ES, Kinsey JH. Photodynamic therapy for early stage squamous cell carcinoma of the lung. *Mayo Clin Proc.* Jul 1997;72(7):595-602. PMID 9212759
17. Spechler SJ, Sharma P, Souza RF, et al. American Gastroenterological Association medical position statement on the management of Barrett's esophagus. *Gastroenterology.* Mar 2011;140(3):1084-1091. PMID 21376940
18. Konda VJ, Waxman I. Endotherapy for Barrett's esophagus. *Am J Gastroenterol.* Jun 2012;107(6):827-833. PMID 22488078
19. Overholt BF, Wang KK, Burdick JS, et al. Five-year efficacy and safety of photodynamic therapy with Photofrin in Barrett's high-grade dysplasia. *Gastrointest Endosc.* Sep 2007;66(3):460-468. PMID 17643436
20. Dunn JM, Mackenzie GD, Banks MR, et al. A randomised controlled trial of ALA vs. Photofrin photodynamic therapy for high-grade dysplasia arising in Barrett's oesophagus. *Lasers Med Sci.* May 2013;28(3):707-715. PMID 22699800
21. Kohoutova D, Haidry R, Banks M, et al. Long-term outcomes of the randomized controlled trial comparing 5-aminolaevulinic acid and Photofrin photodynamic therapy for Barrett's oesophagus related neoplasia. *Scand J Gastroenterol.* 2018 May;53(5):527-532. PMID: 29161901
22. Gao F, Bai Y, Ma SR, et al. Systematic review: photodynamic therapy for unresectable cholangiocarcinoma. *J Hepatobiliary Pancreat Sci.* Mar 2010;17(2):125-131. PMID 19455276
23. Tomizawa Y, Tian J. Photodynamic therapy for unresectable cholangiocarcinoma. *Dig Dis Sci.* Feb 2012;57(2):274-283. PMID 22057285
24. Lu Y, Liu L, Wu JC, et al. Efficacy and safety of photodynamic therapy for unresectable cholangiocarcinoma: A meta-analysis. *Clin Res Hepatol Gastroenterol.* Dec 2015;39(6):718-724. PMID 26070572

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25. Mohan BP, Chandan S, Khan SR, et al. Photodynamic Therapy (PDT), Radiofrequency Ablation (RFA) With Biliary Stents in Palliative Treatment of Unresectable Extrahepatic Cholangiocarcinoma: A Systematic Review and Meta-analysis. *J Clin Gastroenterol*. Feb 01 2022; 56(2): e153-e160. PMID 33780214
26. Ortnor ME, Caca K, Berr F, et al. Successful photodynamic therapy for nonresectable cholangiocarcinoma: a randomized prospective study. *Gastroenterology*. Nov 2003;125(5):1355-1363. PMID 14598251
27. Zoepf T, Jakobs R, Arnold JC, et al. Palliation of nonresectable bile duct cancer: improved survival after photodynamic therapy. *Am J Gastroenterol*. Nov 2005;100(11):2426-2430. PMID 16279895
28. Hauge T, Hauge PW, Warloe T, et al. Randomised controlled trial of temoporfin photodynamic therapy plus chemotherapy in nonresectable biliary carcinoma--PCS Nordic study. *Photodiagnosis Photodyn Ther*. Mar 2016;13:330-333. PMID 26415549
29. Pereira SP, Aithal GP, Ragunath K, et al. Safety and long term efficacy of porfimer sodium photodynamic therapy in locally advanced biliary tract carcinoma. *Photodiagnosis Photodyn Ther*. Dec 2012;9(4):287-292. PMID 23200007
30. Shim CS, Cheon YK, Cha SW, et al. Prospective study of the effectiveness of percutaneous transhepatic photodynamic therapy for advanced bile duct cancer and the role of intraductal ultrasonography in response assessment. *Endoscopy*. May 2005;37(5):425-433. PMID 15844020
31. Harewood GC, Baron TH, Rumalla A, et al. Pilot study to assess patient outcomes following endoscopic application of photodynamic therapy for advanced cholangiocarcinoma. *J Gastroenterol Hepatol*. Mar 2005;20(3):415-420. PMID 15740486
32. Berr F. Photodynamic therapy for cholangiocarcinoma. *Semin Liver Dis*. May 2004;24(2):177-187. PMID 15192790
33. Baron TH. Photodynamic therapy: standard of care for palliation of cholangiocarcinoma? [editorial]. *Clin Gastroenterol Hepatol*. Mar 2008;6(3):266-267. PMID 18328433
34. Godoy H, Vaddadi P, Cooper M, et al. Photodynamic therapy effectively palliates gynecologic malignancies. *Eur J Gynaecol Oncol*. Sep 2013;34(4):300-302. PMID 24020133
35. Choi MC, Jung SG, Park H, et al. Fertility preservation via photodynamic therapy in young patients with early- stage uterine endometrial cancer: a long-term follow-up study. *Int J Gynecol Cancer*. May 2013;23(4):698-704. PMID 23478222
36. Choi MC, Jung SG, Park H, et al. Fertility preservation by photodynamic therapy combined with conization in young patients with early stage cervical cancer: a pilot study. *Photodiagnosis Photodyn Ther*. Sep 2014;11(3):420-425. PMID 24927981
37. Zhang W, Zhang A, Sun W, et al. Efficacy and safety of photodynamic therapy for cervical intraepithelial neoplasia and human papilloma virus infection: A systematic review and meta-analysis of randomized clinical trials. *Medicine (Baltimore)*. May 2018;97(21):e10864. PMID 29794788

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38. Tao XH, Guan Y, Shao D, et al. Efficacy and safety of photodynamic therapy for cervical intraepithelial neoplasia: a systemic review. *Photodiagnosis Photodyn Ther.* Jun 2014;11(2):104-112. PMID 24631593
39. Hillemanns P, Garcia F, Petry KU, et al. A randomized study of hexaminolevulinate photodynamic therapy in patients with cervical intraepithelial neoplasia 1/2. *Am J Obstet Gynecol.* Apr 2015;212(4):465.e461-467. PMID 25467012
40. Istomin YP, Lapzevich TP, Chalau VN, et al. Photodynamic therapy of cervical intraepithelial neoplasia grades II and III with Photolon. *Photodiagnosis Photodyn Ther.* Sep 2010;7(3):144-151. PMID 20728837
41. Soergel P, Dahl GF, Onsrud M, et al. Photodynamic therapy of cervical intraepithelial neoplasia 1-3 and human papilloma virus (HMPV) infection with methylaminolevulinate and hexaminolevulinate--a double-blind, dose-finding study. *Lasers Surg Med.* Jun 2012;44(6):468-474. PMID 22693121
42. Winters U, Daayana S, Lear JT, et al. Clinical and immunologic results of a phase II trial of sequential imiquimod and photodynamic therapy for vulval intraepithelial neoplasia. *Clin Cancer Res.* Aug 15 2008;14(16):5292-5299. PMID 18698049
43. Zhang R, Wang L. Photodynamic therapy for treatment of usual-type vulvar intraepithelial neoplasia: a case report and literature review. *J Int Med Res.* Aug 2019; 47(8): 4019-4026. PMID 31364444
44. Bader MJ, Stepp H, Beyer W, et al. Photodynamic therapy of bladder cancer - a phase I study using hexaminolevulinate (HAL). *Urol Oncol.* Oct 2013;31(7):1178-1183. PMID 22440147
45. Lee JY, Diaz RR, Cho KS, et al. Efficacy and safety of photodynamic therapy for recurrent, high grade nonmuscle invasive bladder cancer refractory or intolerant to bacille Calmette-Guerin immunotherapy. *J Urol.* Oct 2013;190(4):1192-1199. PMID 23648222
46. Gondivkar SM, Gadbaill AR, Choudhary MG, et al. Photodynamic treatment outcomes of potentially-malignant lesions and malignancies of the head and neck region: A systematic review. *J Investig Clin Dent.* May 08 2017. PMID 28480637
47. de Visscher SA, Dijkstra PU, Tan IB, et al. mTHPC mediated photodynamic therapy (PDT) of squamous cell carcinoma in the head and neck: a systematic review. *Oral Oncol.* Mar 2013;49(3):192-210. PMID 23068024
48. Wildeman MA, Nyst HJ, Karakullukcu B, et al. Photodynamic therapy in the therapy for recurrent/persistent nasopharyngeal cancer. *Head Neck Oncol.* Dec 17 2009;1:40. PMID 20017928
49. Karakullukcu B, Stoker SD, Wildeman AP, et al. A matched cohort comparison of mTHPC-mediated photodynamic therapy and trans-oral surgery of early stage oral cavity squamous cell cancer. *Eur Arch Otorhinolaryngol.* Mar 2013;270(3):1093-1097. PMID 22773192
50. Ahn PH, Quon H, O'Malley BW, et al. Toxicities and early outcomes in a phase 1 trial of photodynamic therapy for premalignant and early stage head and neck tumors. *Oral Oncol.* Apr 2016;55:37-42. PMID 26865261

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51. Biel MA. Photodynamic therapy treatment of early oral and laryngeal cancers. *Photochem Photobiol.* Sep-Oct 2007;83(5):1063-1068. PMID 17880501
52. Silbergleit AK, Somers ML, Schweitzer VG, et al. Vocal fold vibration after photofrin-mediated photodynamic therapy for treatment of early-stage laryngeal malignancies. *J Voice.* Nov 2013;27(6):762-764. PMID 24119638
53. Wildeman MA, Fles R, Herdini C, et al. Primary treatment results of Nasopharyngeal Carcinoma (NPC) in Yogyakarta, Indonesia. *PLoS One.* May 2013;8(5):e63706. PMID 23675501
54. Durbec M, Cosmidis A, Fuchsmann C, et al. Efficacy and safety of photodynamic therapy with temoporfin in curative treatment of recurrent carcinoma of the oral cavity and oropharynx. *Eur Arch Otorhinolaryngol.* Mar 2013;270(4):1433-1439. PMID 22927020
55. Rigual NR, Shafirstein G, Frustino J, et al. Adjuvant intraoperative photodynamic therapy in head and neck cancer. *JAMA Otolaryngol Head Neck Surg.* Jul 2013;139(7):706-711. PMID 23868427
56. Rigual NR, Thankappan K, Cooper M, et al. Photodynamic therapy for head and neck dysplasia and cancer. *Arch Otolaryngol Head Neck Surg.* Aug 2009;135(8):784-788. PMID 19687399
57. Schweitzer VG, Somers ML. PHOTOFRIN-mediated photodynamic therapy for treatment of early stage (Tis- T2N0M0) SqCCa of oral cavity and oropharynx. *Lasers Surg Med.* Jan 2010;42(1):1-8. PMID 20077493
58. Lambert A, Nees L, Nuyts S, et al. Photodynamic Therapy as an Alternative Therapeutic Tool in Functionally Inoperable Oral and Oropharyngeal Carcinoma: A Single Tertiary Center Retrospective Cohort Analysis. *Front Oncol.* 2021; 11: 626394. PMID 33747943
59. Muragaki Y, Akimoto J, Maruyama T, et al. Phase II clinical study on intraoperative photodynamic therapy with talaporfin sodium and semiconductor laser in patients with malignant brain tumors. *J Neurosurg.* Oct 2013;119(4):845-852. PMID 23952800
60. Aziz F, Telara S, Moseley H, et al. Photodynamic therapy adjuvant to surgery in metastatic carcinoma in brain. *Photodiagnosis Photodyn Ther.* Sep-Dec 2009;6(3-4):227-230. PMID 19932456
61. Nakamura T, Kusuzaki K, Matsubara T, et al. Long-term clinical outcome in patients with high-grade soft tissue sarcoma who were treated with surgical adjuvant therapy using acridine orange after intra-lesional or marginal resection. *Photodiagnosis Photodyn Ther.* 2018 Sep;23:165-170. PMID: 29885811
62. FNCLCC. The Free Dictionary by Farlex
63. Matsubara T, Kusuzaki K, Matsumine A, et al. Can a less radical surgery using photodynamic therapy with acridine orange be equal to a wide-margin resection? *Clin Orthop Relat Res.* Mar 2013;471(3):792-802. PMID 23008027
64. Matzi V, Maier A, Woltsche M, et al. Polyhematoporphyrin-mediated photodynamic therapy and decortication in palliation of malignant pleural mesothelioma: a clinical pilot study. *Interact Cardiovasc Thorac Surg.* Mar 2004;3(1):52-56. PMID 17670175

MEDICAL POLICY

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

65. Lindenmann J, Matzi V, Neuboeck N, et al. Multimodal therapy of malignant pleural mesothelioma: is the replacement of radical surgery imminent? *Interact Cardiovasc Thorac Surg.* Mar 2013;16(3):237-243. PMID 23171517
66. Friedberg JS, Simone CB, 2nd, Culligan MJ, et al. Extended pleurectomy-decortication-based treatment for advanced stage epithelial mesothelioma yielding a median survival of nearly three years. *Ann Thorac Surg.* Mar 2017;103(3):912-919. PMID 27825687
67. Pereira S. Photodynamic therapy for pancreatic and biliary tract cancer: the United Kingdom experience. *J Natl Compr Canc Netw.* Oct 1 2012;10(Suppl 2):S48-51. PMID 23055216
68. Huggett MT, Jermyn M, Gillams A, et al. Phase I/II study of verteporfin photodynamic therapy in locally advanced pancreatic cancer. *Br J Cancer.* Apr 2 2014;110(7):1698-1704. PMID 24569464
69. Bahng S, Yoo BC, Paik SW, et al. Photodynamic therapy for bile duct invasion of hepatocellular carcinoma. *Photochem Photobiol Sci.* Mar 2013;12(3):439-445. PMID 23175171
70. Vohra F, Al-Kheraif AA, Qadri T, et al. Efficacy of photodynamic therapy in the management of oral premalignant lesions. A systematic review. *Photodiagnosis Photodyn Ther.* Mar 2015;12(1):150-159. PMID 25315968
71. Wisnivesky JP, Yung RC, Mathur PN, et al. Diagnosis and treatment of bronchial intraepithelial neoplasia and early lung cancer of the central airways: Diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest.* May 2013;143(5 Suppl):e263S-277S. PMID 23649442
72. Shaheen NJ, Falk GW, Iyer PG, et al. ACG Clinical Guideline: Diagnosis and Management of Barrett's Esophagus. *Am J Gastroenterol.* Jan 2016;111(1):30-50; quiz 51. PMID 26526079
73. Shaheen NJ, Falk GW, Iyer PG, et al. Diagnosis and Management of Barrett's Esophagus: An Updated ACG Guideline. *Am J Gastroenterol.* Apr 01 2022; 117(4): 559-587. PMID 35354777
74. Sharma P, Shaheen NJ, Katzka D, et al. AGA Clinical Practice Update on Endoscopic Treatment of Barrett's Esophagus With Dysplasia and/or Early Cancer: Expert Review. *Gastroenterology.* Feb 2020; 158(3): 760-769. PMID 31730766
75. Ahmed O, Lee JH, Thompson CC, et al. AGA Clinical Practice Update on the Optimal Management of the Malignant Alimentary Tract Obstruction: Expert Review. *Clin Gastroenterol Hepatol.* Sep 2021; 19(9): 1780-1788. PMID 33813072
76. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Esophageal and esophagogastric junction cancer. Version 3.2024
77. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Biliary tract cancers. Version 2.2024
78. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Non-small cell lung cancer. Version 5.2024
79. National Institute for Health and Care Excellence. Photodynamic therapy for bile duct cancer [IPG134]. 2005; <https://www.nice.org.uk/guidance/ipg134>. Accessed May 26, 2024
80. National Institute for Health and Care Excellence. Photodynamic therapy for localised inoperable endobronchial cancer [IPG137]. 2005

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

81. National Institute for Health and Care Excellence. Photodynamic therapy for advanced bronchial carcinoma [IPG87]. 2004
82. National Institute for Health and Care Excellence. Interstitial photodynamic therapy for malignant parotid tumours [IPG259]. 2008
83. National Institute for Health and Care Excellence. Photodynamic therapy for early-stage oesophageal cancer [IPG200]. 2006
84. National Institute for Health and Care Excellence. Photodynamic therapy for Barrett's oesophagus [IPG350]. 2010
85. National Institute for Health and Care Excellence. Photodynamic therapy for brain tumours [IPG290]. 2009
86. Blue Cross Blue Shield Association Medical Policy Reference Manual. 8.01.06, Oncologic Applications of Photodynamic Therapy, Including Barrett Esophagus. August 2024

Other:

Taber's Cyclopedic Medical Dictionary, 20th edition.

X. Policy HISTORY

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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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