BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:

Confocal Laser Endomicroscopy

Policy #: 520
Latest Review Date: November 2021
Category: Surgery

BACKGROUND:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

POLICY:

Effective for dates of service March 24, 2020 and after:

Blue Advantage will treat the **use of confocal laser endomicroscopy** as a **non-covered benefit** and as **investigational**.

Effective for dates of service on or after February 26, 2018 through March 23, 2020, refer to LCD L36954.

Effective for dates of service prior to February 26, 2018:

Blue Advantage will treat t**he use of confocal laser endomicroscopy as a non-covered benefit** and as i**nvestigational.**

Blue Advantage does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Advantage administers benefits based on the members' contract and medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

DESCRIPTION OF PROCEDURE OR SERVICE:

Confocal laser endomicroscopy (CLE), also known as confocal fluorescent endomicroscopy and optical endomicroscopy, allows in vivo microscopic imaging of cells during endoscopy. Confocal laser endomicroscopy CLE is proposed for a variety of purposes, especially as a real-time alternative to biopsy/polypectomy and histopathologic analysis during colonoscopy and for targeting areas to undergo biopsy in patients with inflammatory bowel disease or Barrett esophagus.

The process of CLE involves light from a low-power laser illuminates tissue and, subsequently, the same lens detects light reflected from the tissue through a pinhole. The term confocal refers to having both illumination and collection systems in the same focal plane. Light reflected and scattered at other geometric angles that is not reflected through the pinhole is excluded from detection which dramatically increases the special resolution of CLE images.

To date, two types of CLE systems have been cleared by the U.S. Food and Drug Administration (FDA). One is an endoscope-based system in which a confocal probe is incorporated onto the tip of a conventional endoscope. The other is a probe-based system; the probe is placed through the biopsy channel of a conventional endoscope. The depth of view is up to 250 µm with the endoscopic system and about 120 µm with the probe-based system. A limited area can be examined; no more than 700 µm in the endoscopic-based system and less with the probe-based system. As pointed out in systematic reviews, the limited viewing area emphasizes the need for

careful conventional endoscopy to target the areas for evaluation. Both CLE systems are optimized using a contrast agent. The most widely used agent is intravenous fluorescein, which is FDA-approved for ophthalmologic imaging of blood vessels when used with a laser scanning ophthalmoscope.

Unlike techniques such as chromoendoscopy (see Medical Policy # 494- Chromoendoscopy as an Adjunct to Colonoscopy), which are primarily intended to improve the sensitivity of colonoscopy, CLE is unique in that it is designed to characterize the cellular structure of lesions immediately. Confocal laser endomicroscopy can thus potentially be used to make a diagnosis of polyp histology, particularly in association with screening or surveillance colonoscopy, which could allow for small hyperplastic lesions to be overlooked rather than removed and sent for histologic evaluation. Using CLE would reduce risks associated with biopsy and reduce the number of biopsies and histologic evaluations.

Another potential application of CLE technology is targeting areas for biopsy in patients with Barrett esophagus undergoing surveillance endoscopy. CLE would be proposed as an alternative to the current standard approach, recommended by the American Gastroenterological Association, which is that patients with Barrett esophagus who do not have dysplasia undergo endoscopic surveillance every 3 to 5 years. The American Gastroenterological Association has further recommended that random 4-quadrant biopsies every 2 cm be taken with white-light endoscopy in patients without known dysplasia.

Other potential uses of CLE under investigation include better diagnosis and differentiation of conditions such as gastric metaplasia, lung cancer and bladder cancer.

As noted, limitations of CLE systems include a limited viewing area and depth of view. Another issue is the standardization of systems for classifying lesions viewed with CLE devices. Although there is not currently an internationally accepted classification system for colorectal lesions, two systems have been developed that have been used in a number of studies conducted in different countries. These include the Mainz criteria for endoscopy-based CLE devices and the Miami classification system for probe-based CLE devices. Lesion classification systems are less developed for non-gastrointestinal lesions viewed by CLE devices e.g., those in the lung or bladder. Another challenge is the learning curve for obtaining high-quality images and classifying lesions. Several studies, however, have found that the ability to acquire high-quality images and interpret them accurately can be learned relatively quickly; these studies were specific to colorectal applications of CLE.

KEY POINTS:

The most recent literature review was updated through September 29, 2021.

Summary of Evidence

For individuals who have suspected or known colorectal lesions who receive CLE as an adjunct to colonoscopy, the evidence includes multiple diagnostic accuracy studies. The relevant outcomes are overall survival, disease-specific survival, test validity, other test performance

measures and resource utilization. In 3 published systematic reviews, pooled estimates of overall sensitivity of CLE ranged from 81% to 94%, and pooled estimates of the specificity ranged from 88% to 95%. It is uncertain whether the accuracy is sufficiently high to replace biopsy/polypectomy and histopathologic analysis. Moreover, issues remain concerning the use of this technology in clinical practice (eg, the learning curve, interpretation of lesions). The evidence is insufficient to determine that the technology results in improvement in the net health outcome.

For individuals who have Barrett esophagus who are undergoing surveillance who receive CLE with targeted biopsy, the evidence includes several randomized controlled trials (RCTs) and 2 meta-analyses. The relevant outcomes are OS, disease-specific survival, test validity, other test performance measures and resource utilization. Evidence from RCTs has suggested that CLE is more sensitive than standard endoscopy for identifying areas of dysplasia. However, a 2014 meta-analysis found that the pooled sensitivity, specificity, and negative predictive value of available studies were not sufficiently high to replace the standard surveillance protocol. National guidelines continue to recommend 4-quadrant random biopsies for patients with Barrett esophagus undergoing surveillance. The single RCT, which compared high-definition white-light endoscopy with high-definition white-light endoscopy plus CLE, was stopped early because an interim analysis did not find a between-group difference in outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have gastrointestinal lesions who have received endoscopic treatment who receive CLE to assess the adequacy of endoscopic treatment, the evidence includes a systematic review that includes a single RCT and 2 prospective, nonrandomized studies. The relevant outcomes are overall survival, disease-specific survival, test validity, and resource utilization. The evidence is insufficient to determine the the technology results in an improvement in the net health outcome.

For individuals who have who have a suspicion of a condition diagnosed by identification and biopsy of lesions (e.g., lung, bladder or gastric cancer) who receive CLE, the evidence mainly consists of a small number of diagnostic accuracy studies. The relevant outcomes are overall survival, disease-specific survival, test validity, other test performance measures and resource utilization. There is limited evidence on diagnostic accuracy for any of these other indications. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

American Society for Gastrointestinal Endoscopy

The American Society for Gastrointestinal Endoscopy (2006; reaffirmed in 2011) published guidelines on the role of endoscopy in the surveillance of premalignant conditions of the upper gastrointestinal (GI) tract. Regarding the use of confocal endoscopy as an adjunct to white-light endoscopy, the guidelines stated that this technique is “still in development.”

In 2019, the ASGE published a guideline on screening and surveillance of Barrett esophagus (BE) which recommends against routine use of confocal laser endomicroscopy (CLE) compared with white-light endoscopy with Seattle protocol biopsy sampling in patients with BE undergoing surveillance. An older guideline from the Society (2012) on the role of endoscopy in BE and other premalignant conditions of the esophagus stated the following:

"Adjuncts to white-light endoscopy used to improve the sensitivity for the detection of BE and dysplastic BE include chromoendoscopy, electrical enhanced imaging, magnification, and confocal endoscopy."

In 2014, the ASGE published a technology status evaluation on CLE. It concluded that CLE is an emerging technology with the potential to improve patient care. However, before it can be widely accepted, further studies are needed in the following areas:

1. "[T]he applicability and practicality of CLE, especially in community settings…...Although current studies of CLE seem promising, these have primarily been in academic centers, and their generalizability in nonacademic practices is unknown."
2. The "learning curve of CLE image interpretation, use of CLE devices, and additional time needed to perform the procedure…."
3. The clinical efficacy of the technology … compared with other available advanced imaging technologies…."
4. Improvements in CLE imaging and image interpretation…."

The ASGE published guidelines on the role of endoscopy in benign pancreatic disease in 2015 and stated that "confocal endomicroscopy is an emerging technology that may prove useful for the evaluation of indeterminate pancreatic strictures." Similarly, in the ASGE's 2016 guidelines on the role of endoscopy in the diagnosis and treatment of cystic pancreatic neoplasms, they acknowledged that CLE was an emerging technique for pancreatic lesion evaluation, but made no formal recommendations regarding its use.

American Gastroenterological Association

The American Gastroenterological Association (2011) published a position statement on the management of BE. The statement included the following recommendations on endoscopic surveillance of BE (see Table 1).

Table 1. Recommendations on Endoscopic Surveillance of Barrett Esophagus

Recommendation	LOR	QOE
"We [the guideline developers] suggest that endoscopic surveillance be performed in patients with Barrett's esophagus."	Weak	Moderate
"We [the guideline developers] suggest the following surveillance intervals: No dysplasia: 3-5 years	Weak	Low

Low-grade dysplasia: 6-12 months High-grade dysplasia in the absence of eradication therapy: 3 months"		
"For patients with Barrett's esophagus who are undergoing surveillance, we [the guideline developers] recommend: Endoscopic evaluation be performed using white-light endoscopy. 4-quadrant biopsy specimens be taken every 2 cm. Specific biopsy specimens of any mucosal irregularities be submitted separately to the pathologist. 4-quadrant biopsy specimens be obtained every 1 cm in patients with known or suspected dysplasia."	Strong Strong Strong Strong	Moderate Moderate Moderate Moderate
"We [the guideline developers] suggest against requiring chromoendoscopy or advanced imaging techniques for the routine surveillance of patients with Barrett's esophagus at this time."	Weak	Low

LOR: level of recommendation; QOE: quality of evidence.

U.S. Preventive Services Task Force Recommendations
The U.S. Preventive Services Task Force recommendations on colorectal cancer screening do not mention CLE.

KEY WORDS:
Confocal laser endomicroscopy, confocal fluorescent endomicroscopy, Optical endomicroscopy, Pentax Confocal Laser System, Cellvizio, CLE, CranioFlex™ Confocal Miniprobe

APPROVED BY GOVERNING BODIES:
Two confocal laser endomicroscopy (CLE) devices have been cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process.

Cellvizio (Mauna Kea Technologies; Paris, France): This is a confocal microscopy device with a fiber optic probe (i.e., a probe-based CLE system). The device consists of a laser scanning unit, proprietary software, a flat-panel display and miniaturized fiber optic probes. The F-600 system, cleared by the FDA in 2006, can be used with any standard endoscope with a working channel of at least 2.8 mm. According to the FDA documents, the device is intended for confocal laser imaging of the internal microstructure of tissues in the anatomical tract (gastrointestinal or respiratory) that are accessed by an endoscope. The 100 series version of the system (F400-v2) was cleared by the FDA in 2015 for imaging of the internal microstructure of tissues and for visualization of body cavities, organs, and canals during endoscopic and laparoscopic surgery, and has been approved for use with several miniprobes for specific indications. Confocal Miniprobes™ approved for use with the Cellvizio 100 series that are particularly relevant to this

review include the GastroFlex™ and ColoFlex™ (for imaging of anatomical tracts, i.e., gastrointestinal systems, accessed by an endoscope or endoscopic accessories), and the CranioFlex™ for visualization within the central nervous system during cranial diagnostic and therapeutic procedures such as tumor biopsy and resection)." In 2020, the Cellvizio 100 series system received extended FDA approval to allow for use of fluorescein sodium as a contrast agent for visualization of blood flow for all of its approved indications. Later in 2020, the Cellvizio I.V.E. system with Confocal Miniprobes was approved by the FDA as a newer version of the previously approved 100 series system, designed to reduce the system footprint and improve device usability. The 2 devices are otherwise equivalent and are approved for the same indications.

Confocal Video Colonoscope (Pentax Medical Company: Montvale, NJ): This is an endoscopy-based CLE system. The EC-3870CILK system, cleared by the FDA in 2004, is used with a Pentax Video Processor and with a Pentax Confocal Laser System. According to the FDA materials, the intended use of the device is to provide optical and microscopic visualization of and therapeutic access to the lower gastrointestinal tract.

Table 2. Endomicroscopy Devices Cleared by the U.S. Food and Drug Administration

Device	Manufacturer	Date Cleared	510 (k) No.	Indication
Cellvizio 100 Series Confocal Laser Imaging Systems And Their Confocal Miniprobes	Mauna Kea Technologies	02/22/2019	K183640	For use in endomicroscopy
Ec-3870clik, Confocal Video Colonoscope	Pentax Medical Company	10/19/2004	K042741	For use in endomicroscopy

BENEFIT APPLICATION:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

CURRENT CODING:

CPT Codes:

43206	Esophagoscopy, flexible, transoral; with optical endomicroscopy
43252	Esophagogastroduodenoscopy, flexible, transoral: with optical endomicroscopy
88375	Optical endomicroscopic image(s), interpretation and report, real-time or referred,

	each endoscopic session
0397T	Endoscopic retrograde cholangiopancreatography (ERCP), with optical endomicroscopy (List separately in addition to code for primary procedure) (Effective January 1, 2016)

*NOTE: Code 88375 cannot be reported in conjunction with codes 43206 and 43252

REFERENCES:

1. American Gastroenterological Association, Spechler SJ, Sharma P, et al. American Gastroenterological Association medical position statement on the management of Barrett's esophagus. Gastroenterology. Mar 2011; 140(3):1084-1091.
2. American Society for Gastrointestinal Endoscopy Technology Committee. Confocal laser endomicroscopy. Available online at: www.asge.org/uploadedFiles/Publications_and_Products/Practice_Guidelines/confocal.pdf.
3. American Society for Gastrointestinal Endoscopy. The role of endoscopy in the surveillance of premalignant conditions of the upper GI tract. www.guideline.gov. Accessed October 2016.
4. ASGE Technology Committee. Confocal laser endomicroscopy. Gastrointest Endosc. Dec 2014;80(6):928-938.
5. Beji S, Wrist Lam G, Ostergren PB, et al. Diagnostic value of probe-based confocal laser endomicroscopy versus conventional endoscopic biopsies of non-muscle invasive bladder tumors: a pilot study. Scand J Urol. Feb 2021; 55(1): 36-40.
6. Bertani H, Frazzoni M, Dabizzi E et al. Improved detection of incident dysplasia by probe-based confocal laser endomicroscopy in a Barrett's esophagus surveillance program. Dig Dis Sci 2012. [Epub ahead of print]
7. Bok GH, Jeon SR, Cho JY et al. The accuracy of probe-based confocal endomicroscopy versus conventional endoscopic biopsies for the diagnosis of superficial gastric neoplasia (with videos). Gastrointest Endosc 2013; 77(6):899-908.
8. Buchner AM, Gomez V, Heckman MG et al. The learning curve of in vivo probe-based confocal laser endomicroscopy for prediction of colorectal neoplasia. Gastrointest Endosc 2011; 73(3):556-60.
9. Buchner AM, Shahid MW, Heckman MG et al. Comparison of probe-based confocal laser endomicroscopy with virtual chromoendoscopy for classification of colon polyps. Gastroenterology 2010; 138(3):834-42.
10. Canto MI, Anandasabapathy S, Brugge W, et al. In vivo endomicroscopy improves detection of Barrett's esophagus-related neoplasia: a multicenter international randomized controlled trial (with video). Gastrointest Endosc. Feb 2014;79(2):211-221.
11. Chauhan SS, Dayyeh BK, Bhat YM, et al. Confocal laser endomicroscopy. Gastrointest Endosc. Dec 2014; 80(6): 928-38.richardson

12. Davidson KW, Barry MJ, Mangione CM, et al. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. JAMA. May 18 2021; 325(19): 1965-1977.
13. De Palma GD, Esposito D, Luglio G, et al. Confocal laser endomicroscopy in breast surgery: a pilot study. BMC Cancer. 2015; 15:252.
14. Dong YY, Li YQ, Yu YB et al. Meta-analysis of confocal laser endomicroscopy for the detection of colorectal neoplasia. Colorectal Dis 2013; 15(9):e488-95.
15. Dunbar KB, Okolo P, 3rd, Montgomery E et al. Confocal laser endomicroscopy in Barrett's esophagus and endoscopically inapparent Barrett's neoplasia: a prospective, randomized, double-blind, controlled, crossover trial. Gastrointest Endosc 2009; 70(4):645-54.
16. Evans JA, Early DS, Fukami N et al. The role of endoscopy in Barrett's esophagus and other premalignant conditions of the esophagus. Gastrointest. Endosc., 2012 Nov 21;76(6).
17. Facciorusso A, Buccino VR, Sacco R. Needle-based confocal laser endomicroscopy in pancreatic cysts: a meta-analysis. Eur J Gastroenterol Hepatol. Sep 2020; 32(9): 1084-1090.
18. Fuchs FS, Zirlik S, Hildner K et al. Confocal laser endomicroscopy for diagnosing lung cancer in vivo. Eur Resp J 2012. [Epub ahead of print]
19. Fuchs FS, Zirlik S, Hildner K, et al. Confocal laser endomicroscopy for diagnosing lung cancer in vivo. Eur Respir J. Jun 2013;41(6):1401-1408.
20. Guo J, Li CQ, Li M, et al. Diagnostic value of probe-based confocal laser endomicroscopy and high-definition virtual chromoendoscopy in early esophageal squamous neoplasia. Gastrointest Endosc. Jun 2015; 81(6):1346-1354.
21. Gupta A, Attar BM, Koduru P, et al. Utility of confocal laser endomicroscopy in identifying high-grade dysplasia and adenocarcinoma in Barrett's esophagus: a systematic review and meta-analysis. Eur J Gastroenterol Hepatol. Apr 2014; 26 (4): 369-377.
22. Han S, Kahaleh M, Sharaiha RZ, et al. Probe-based confocal laser endomicroscopy in the evaluation of dominant strictures in patients with primary sclerosing cholangitis: results of a U.S. multicenter prospective trial. Gastrointest Endosc. Sep 2021; 94(3): 569-576.e1.
23. Hao S, Ding W, Jin Y, et al. Appraisal of EUS-guided needle-based confocal laser endomicroscopy in the diagnosis of pancreatic lesions: A single Chinese center experience. Endosc Ultrasound. May-Jun 2020; 9(3): 180-186.
24. He XK, Liu D, Sun LM. Diagnostic performance of confocal laser endomicroscopy for optical diagnosis of gastric intestinal metaplasia: a meta-analysis. BMC Gastroenterol. Sep 05 2016; 16:109.
25. Hirota WK, Zuckerman MJ, Adler DG et al. ASGE guideline: the role of endoscopy in the surveillance of premalignant conditions of the upper GI tract. 2006. Available online at: www.guideline.gov.
26. Hirota WK, Zuckerman MJ, Adler DG, et al. ASGE guideline: the role of endoscopy in the surveillance of premalignant conditions of the upper GI tract. Gastrointest Endosc. Apr 2006;63(4):570-580.

27. Hlavaty T, Huorka M, Koller T et al. Colorectal cancer screening in patients with ulcerative and Crohn's colitis with use of colonoscopy, chromoendoscopy and confocal endomicroscopy. Eur J Gastroenterol Hepatol 2011; 23(8):680-9.
28. IOM (Institute of Medicine). 2011. Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press.
29. Karia K, Waxman I, Konda VJ, et al. Needle-based confocal endomicroscopy for pancreatic cysts: the current agreement in interpretation. Gastrointest Endosc. Sep 14 2015.
30. Karia K, Waxman I, Konda VJ, et al. Needle-based confocal endomicroscopy for pancreatic cysts: the current agreement in interpretation. Gastrointest Endosc. May 2016;83(5):924-927.
31. Krishna SG, Hart PA, Malli A, et al. Endoscopic Ultrasound-Guided Confocal Laser Endomicroscopy Increases Accuracy of Differentiation of Pancreatic Cystic Lesions. Clin Gastroenterol Hepatol. Feb 2020; 18(2): 432-440.e6.
32. Li WB, Zuo XL, Li CQ et al. Diagnostic value of confocal laser endomicroscopy for gastric superficial cancerous lesions. Gut 2011; 60(3):299-306.
33. Li Z, Zuo XL, Yu T, et al. Confocal laser endomicroscopy for in vivo detection of gastric intestinal metaplasia: a randomized controlled trial. Endoscopy. Apr 2014; 46 (4): 282-290.
34. Lim LG, Yeoh KG, Srivastava S et al. Comparison of probe-based confocal endomicroscopy with virtual chromoendoscopy and white-light endoscopy for diagnosis of gastric intestinal metaplasia. Surg Endosc 2013; 27(12):4649-55.
35. Lin JS, Piper MA, Perdue LA, et al. Screening for colorectal cancer: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA. Jun 21 2016;315(23):2576-2594.
36. Liu J, Li M, Li Z, et al. Learning curve and interobserver agreement of confocal laser endomicroscopy for detecting precancerous or early-stage esophageal squamous cancer. PLoS One. 2014;9(6):e99089.
37. Liu J, Li M, Li Z, et al. Learning curve and interobserver agreement of confocal laser endomicroscopy for detecting precancerous or early-stage esophageal squamous cancer. PLoS One. 2014; 9(6): e99089.
38. Liu JJ, Droller MJ, Liao JC. New optical imaging technologies for bladder cancer: considerations and perspectives. J Urol 2012; 188(2):361-8.
39. Liu T, Zheng H, Gong W, et al. The accuracy of confocal laser endomicroscopy, narrow band imaging, and chromoendoscopy for the detection of atrophic gastritis. J Clin Gastroenterol. May-Jun 2015; 49(5):379-386.
40. Martinek J, Kollar M, Krajciova J, et al. Confocal laser endomicroscopy in diagnosing indeterminate biliary strictures and pancreatic lesions a prospective pilot study. Rozhl Chir. 2020; 99(6): 258-265.
41. Moore C, Mehta V, Ma X, et al. Interobserver agreement of confocal laser endomicroscopy for detection of head and neck neoplasia. Laryngoscope. Sep 15 2015.

42. Moore C, Mehta V, Ma X, et al. Interobserver agreement of confocal laser endomicroscopy for detection of head and neck neoplasia. Laryngoscope. Mar 2016;126(3):632-637.
43. Nakaoka K, Hashimoto S, Kawabe N, et al. Probe-based confocal laser endomicroscopy for the diagnosis of pancreatic ductal structures. J Gastroenterol Hepatol. Jan 2021; 36(1): 118-124.
44. Napoleon B, Lemaistre AI, Pujol B, et al. In vivo characterization of pancreatic cystic lesions by needle-based confocal laser endomicroscopy (nCLE): proposition of a comprehensive nCLE classification confirmed by an external retrospective evaluation. Surg Endosc. Oct 1 2015.
45. Napoleon B, Lemaistre AI, Pujol B, et al. In vivo characterization of pancreatic cystic lesions by needle-based confocal laser endomicroscopy (nCLE): proposition of a comprehensive nCLE classification confirmed by an external retrospective evaluation. Surg Endosc. Jun 2016;30(6):2603-2612.
46. Nathan CA, Kaskas NM, Ma X, et al. Confocal Laser Endomicroscopy in the Detection of Head and Neck Precancerous Lesions. Otolaryngol Head Neck Surg. Apr 3 2014; 151 (1): 73-80.
47. Neumann H, Vieth M, Atreya R et al. Prospective evaluation of the learning curve of confocal laser endomicroscopy in patients with IBD. Histol Histopathol 2011; 26(7):867-72.
48. Park CH, Kim H, Jo JH et al. Role of probe-based confocal laser endomicroscopy-targeted biopsy in the molecular and histopathological study of gastric cancer. J. Gastroenterol. Hepatol., 2018 Sep 18;34(1).
49. Qian W, Bai T, Wang H, et al. Meta-analysis of confocal laser endomicroscopy for the diagnosis of gastric neoplasia and adenocarcinoma. J Dig Dis. Jun 2016; 17(6):366-376.
50. Qumseya B, Sultan S, Bain P, et al. ASGE guideline on screening and surveillance of Barrett's esophagus. Gastrointest Endosc. Sep 2019; 90(3): 335-359.e2.
51. Richardson C, Colavita P, Dunst C, et al. Real-time diagnosis of Barrett's esophagus: a prospective, multicenter study comparing confocal laser endomicroscopy with conventional histology for the identification of intestinal metaplasia in new users. Surg Endosc. May 2019; 33(5): 1585-1591.
52. Salvatori F, Siciliano S, Maione F et al. Confocal Laser Endomicroscopy in the Study of Colonic Mucosa in IBD Patients: A Review. Gastroenterol Res Pract 2012; 2012:525098.
53. Schueler SA, Gamble LA, Curtin BF, et al. Evaluation of confocal laser endomicroscopy for detection of occult gastric carcinoma in CDH1 variant carriers. J Gastrointest Oncol. Apr 2021; 12(2): 216-225.
54. Shahid MW, Buchner AM, Raimondo M et al. Accuracy of real-time vs. blinded offline diagnosis of neoplastic colorectal polyps using probe-based confocal laser endomicroscopy: a pilot study. Endoscopy 2012; 44(4):343-8.
55. Sharma P, Meining AR, Coron E et al. Real-time increased detection of neoplastic tissue in Barrett's esophagus with probe-based confocal laser endomicroscopy: final results of

an international multicenter, prospective, randomized, controlled trial. Gastrointest Endosc 2011; 74(3):465-72.

56. Slivka A, Gan I, Jamidar P, et al. Validation of the diagnostic accuracy of probe-based confocal laser endomicroscopy for the characterization of indeterminate biliary strictures: results of a prospective multicenter international study. Gastrointest Endosc. Feb 2015; 81(2):282-290.
57. Smith I, Kline PE, Gaidhane M et al. A review on the use of confocal laser endomicroscopy in the bile duct. Gastroenterol Res Pract 2012; 2012:454717.
58. Sonn GA, Jones SN, Tarin TV et al. Optical biopsy of human bladder neoplasia with in vivo confocal laser endomicroscopy. J Urol 2009; 182(4):1299-1305.
59. Sorokina A, Danilevskaya O, Averyanov A, et al. Comparative study of ex vivo probe-based confocal laser endomicroscopy and light microscopy in lung cancer diagnostics. Respirology. Aug 2014; 19 (6): 907-913.
60. Spechler SJ, Sharma P, Souza RF et al. American Gastroenterological Association medical position statement on the management of Barrett's esophagus. 2011. Available online at: www.guideline.gov. Accessed October 2016.
61. Sponsored by National University Hospital (Singapore). Comparison between probe-based confocal laser endomicroscopy, white-light endoscopy and virtual chromoendoscopy (pCLE-GCEP) (NCT01398579). Available online at: clinicaltrials.gov. Last accessed December, 2012.
62. Sponsored by Shandong University. Confocal laser endomicroscopy for the diagnosis of gastric intestinal metaplasia, intraepithelial neoplasia, and carcinoma (NCT01642797). Available online at: clinicaltrials.gov. Last accessed December, 2012.
63. Su P, Liu Y, Lin S et al. Efficacy of confocal laser endomicroscopy for discriminating colorectal neoplasms from non-neoplasms: a systematic review and meta-analysis. Colorectal Dis 2012. [Epub ahead of print]
64. Wallace MB, Crook JE, Saunders M, et al. Multicenter, randomized, controlled trial of confocal laser endomicroscopy assessment of residual metaplasia after mucosal ablation or resection of GI neoplasia in Barrett's esophagus. Gastrointest Endosc. Sep 2012; 76 (3): 539-547 e531.
65. Wanders LK, East JE, Uitentuis SE et al. Diagnostic performance of narrowed spectrum endoscopy, autofluorescence imaging, and confocal laser endomicroscopy for optical diagnosis of colonic polyps: a meta-analysis. Lancet Oncol 2013; 14(13):1337-47.
66. Wang SF, Yang YS, Wei LX et al. Diagnosis of gastric intraepithelial neoplasia by narrow-band imaging and confocal laser endomicroscopy. World J Gastroenterol 2012; 18(34):4771-80.
67. Wellikoff AS, Holladay RC, Downie GH, et al. Comparison of in vivo probe-based confocal laser endomicroscopy with histopathology in lung cancer: A move toward optical biopsy. Respirology. Aug 2015; 20(6):967-974.
68. Wu J, Pan YM, Wang TT et al. Confocal laser endomicroscopy for detection of neoplasia in Barrett's esophagus: a meta-analysis. Dis Esophagus 2013.

69. Wu J, Wang YC, Luo WJ, et al. Diagnostic Performance of Confocal Laser Endomicroscopy for the Detection of Bladder Cancer: Systematic Review and Meta-Analysis. Urol Int. 2020; 104(7-8): 523-532.
70. Xie XJ, Li CQ, Zuo XL et al. Differentiation of colonic polyps by confocal laser endomicroscopy. Endoscopy 2011; 43(2):87-93.
71. Xiong YQ, Ma SJ, Zhou JH, et al. A meta-analysis of confocal laser endomicroscopy for the detection of neoplasia in patients with Barrett's esophagus. J Gastroenterol Hepatol. Jun 2016; 31(6):1102-1110.
72. Ypsilantis E, Pissas D, Papagrigoriadis S, et al. Use of confocal laser endomicroscopy to assess the adequacy of endoscopic treatment of gastrointestinal neoplasia: a systematic review and meta-analysis. Surg Laparosc Endosc Percutan Tech. Feb 2015;25(1):1-5.
73. Zuo XL, Li Z, Li CQ et al. Probe-based endomicroscopy for in vivo detection of gastric intestinal metaplasia and neoplasia: a multicenter randomized controlled trial. Endoscopy, 2017 Jul 29;49(11).

POLICY HISTORY:

Adopted for Blue Advantage, February 2013
Available for comment February 21 through April 7, 2013
Medical Policy Group, December 2013
Medical Policy Group, January 2014
Medical Policy Group, January 2015
Medical Policy Group, December 2015
Medical Policy Group, January 2017
Medical Policy Group, December 2017
Medical Policy Group, February 2018
Medical Policy Group, April 2020: Reinstated effective March 24, 2020.
Medical Policy Group, November 2021