



## FEP Medical Policy Manual

### FEP 2.01.87 Confocal Laser Endomicroscopy

**Annual Effective Policy Date: April 1, 2024**

**Original Policy Date: March 2013**

**Related Policies:**

- 2.01.84 - Chromoendoscopy as an Adjunct to Colonoscopy
- 6.01.32 - Virtual Colonoscopy/Computed Tomography Colonography

## Confocal Laser Endomicroscopy

### Description

#### Description

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 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.

#### OBJECTIVE

The objective of this evidence review is to determine whether the use of confocal laser endomicroscopy improves the net health outcome compared with standard diagnostic or disease monitoring procedures.

## POLICY STATEMENT

Use of confocal laser endomicroscopy is considered **investigational**.

## POLICY GUIDELINES

None

## BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

## FDA REGULATORY STATUS

Two CLE devices have been cleared for marketing by the FDA through the 510(k) process.

Cellvizio (Mauna Kea Technologies) is a confocal microscopy device with a fiber optic probe (ie, 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, the device is intended for imaging the internal microstructure of tissues in the anatomic 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 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 miniproboscopes for specific indications. Confocal Miniproboscopes™ 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 [ie, 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 Miniproboscopes 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. In 2022, the Cellvizio 100 series system F800 model received extended FDA approval to allow for use of indocyanine green (ICG) and pafolacianine as contrast agents. Intravenous administration of ICG is used to perform fluorescence angiography and interstitial administration of ICG is used to perform fluorescence imaging and visualization of the lymphatic system. Intravenous administration of pafolacianine is used to perform fluorescence imaging of tissues. FDA product codes: GCJ, GWG, OWN.

Confocal Video Colonoscope (Pentax Medical) is an endoscopy-based CLE system. The EC-38 70 CILK 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, the device is intended to provide optical and microscopic visualization of and therapeutic access to the lower gastrointestinal tract. FDA product code: GCJ/DFD (endoscope and accessories). This device is no longer commercially available from the manufacturer.

**Table 1. 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 Miniproboscopes	Mauna Kea Technologies	02/22/2019	K183640	For use in endomicroscopy
Ec-3870cilk, Confocal Video Colonoscope	Pentax Medical Company	10/19/2004	K042741	For use in endomicroscopy

## RATIONALE

### Summary of Evidence

For individuals who have suspected or known colorectal lesions who receive confocal laser endomicroscopy (CLE) as an adjunct to colonoscopy, the evidence includes multiple diagnostic accuracy studies. Relevant outcomes are overall survival (OS), disease-specific survival, test validity, and resource utilization. In 3 published systematic reviews, pooled estimates of the 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 an improvement in the net health outcome.

For individuals who have Barrett esophagus (BE) who are undergoing surveillance and receive CLE with targeted biopsy, the evidence includes several randomized-controlled trials (RCTs) and meta-analyses. Relevant outcomes are OS, disease-specific survival, test validity, and resource utilization. Evidence from RCTs has suggested that CLE has similar or higher sensitivity than standard endoscopy for identifying areas of dysplasia. However, a 2014 meta-analysis found that the pooled sensitivity, specificity, and negative predictive value (NPV) of available studies were not sufficiently high to replace the standard surveillance protocol. In a 2022 meta-analysis, the absolute increase in neoplasia detection using CLE compared with the Seattle protocol randomized biopsies was 5%. Additionally, dysplasia prevalence was 4% with Seattle protocol randomized biopsies and 9% with CLE. National guidelines continue to recommend 4-quadrant random biopsies for patients with BE undergoing surveillance. One 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 and have had 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. Relevant outcomes are OS, disease-specific survival, test validity, and resource utilization. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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

## SUPPLEMENTAL INFORMATION

### Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

#### American Society for Gastrointestinal Endoscopy

The American Society for Gastrointestinal Endoscopy (ASGE, 2006; reaffirmed in 2011) published guidelines on the role of endoscopy in the surveillance of premalignant conditions of the upper gastrointestinal (GI) tract.<sup>53</sup> 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.<sup>12</sup> 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."<sup>54</sup>

In 2014, the ASGE published a technology status evaluation on CLE.<sup>13</sup> 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."<sup>55</sup> 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.<sup>56</sup>

## American Gastroenterological Association

In 2011, the American Gastroenterological Association (AGA) published a position statement on the management of BE.<sup>1</sup> The statement included the following recommendations on endoscopic surveillance of BE (see Table 2).

**Table 2. 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: <ul style="list-style-type: none"> <li>• No dysplasia: 3-5 years</li> <li>• Low-grade dysplasia: 6-12 months</li> <li>• High-grade dysplasia in the absence of eradication therapy: 3 months"</li> </ul>	Weak	Low
"For patients with Barrett's esophagus who are undergoing surveillance, we [the guideline developers] recommend: <ul style="list-style-type: none"> <li>• Endoscopic evaluation be performed using white-light endoscopy.</li> <li>• 4-quadrant biopsy specimens be taken every 2 cm.</li> <li>• Specific biopsy specimens of any mucosal irregularities be submitted separately to the pathologist.</li> <li>• 4-quadrant biopsy specimens be obtained every 1 cm in patients with known or suspected dysplasia."</li> </ul>	Strong (for all)	Moderate (for all)
"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.

In 2016, the AGA published a clinical practice update expert review on the diagnosis and management of low-grade dysplasia in BE.<sup>57</sup> Regarding the use of other advanced endoscopic imaging techniques, the guideline stated that the use of confocal laser endomicroscopy "cannot be recommended in the routine clinical management" of patients undergoing surveillance.

In 2022, the AGA published a clinical practice update on new technology for surveillance and screening in BE.<sup>58</sup> The article makes the following best practice advice statement relevant to screening and surveillance for BE:

- "Screening and surveillance endoscopic examination should be performed using high-definition white light endoscopy and virtual chromoendoscopy, with endoscopists spending adequate time inspecting the Barrett's segment."

None of the best practice advice statements mentioned CLE. While the article did summarize data in support of innovative screening technologies such as CLE, the panelists noted that: "the use of these techniques was not required for a high-quality exam and the data to date did not support its routine use." However, the panelists also noted that "these technologies were promising and carried potential benefits in select cases and currently might be best utilized in expert centers."

## U.S. Preventive Services Task Force Recommendations

The **U.S. Preventive Services Task Force** recommendations on colorectal cancer screening do not mention CLE.<sup>59</sup>

## Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

## REFERENCES

1. 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): 1084-91. PMID 21376940
2. 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. PMID 22474440
3. Neumann H, Vieth M, Atreya R, et al. Prospective evaluation of the learning curve of confocal laser endomicroscopy in patients with IBD. *Histol Histopathol*. Jul 2011; 26(7): 867-72. PMID 21630216
4. 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*. Mar 2011; 73(3): 556-60. PMID 21353852
5. 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*. Jan 2013; 15(1): e1-12. PMID 23006609
6. Dong YY, Li YQ, Yu YB, et al. Meta-analysis of confocal laser endomicroscopy for the detection of colorectal neoplasia. *Colorectal Dis*. Sep 2013; 15(9): e488-95. PMID 23810105
7. 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*. Dec 2013; 14(13): 1337-47. PMID 24239209
8. Xie XJ, Li CQ, Zuo XL, et al. Differentiation of colonic polyps by confocal laser endomicroscopy. *Endoscopy*. Feb 2011; 43(2): 87-93. PMID 21038291
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*. Mar 2010; 138(3): 834-42. PMID 19909747
10. 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*. Apr 2012; 44(4): 343-8. PMID 22382851
11. 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*. Aug 2011; 23(8): 680-9. PMID 21602687
12. 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. PMID 31439127
13. Chauhan SS, Dayyeh BK, Bhat YM, et al. Confocal laser endomicroscopy. *Gastrointest Endosc*. Dec 2014; 80(6): 928-38. PMID 25442092
14. DeMeester S, Wang K, Ayub K, et al. High-definition probe-based confocal laser endomicroscopy review and meta-analysis for neoplasia detection in Barrett's esophagus. *Techniques and Innovations in Gastrointestinal Endoscopy*. 2022;24(4):340-350.
15. 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): 1102-10. PMID 26676646
16. 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): 369-77. PMID 24535597
17. Vithayathil M, Modolell I, Ortiz-Fernandez-Sordo J, et al. Image-Enhanced Endoscopy and Molecular Biomarkers Vs Seattle Protocol to Diagnose Dysplasia in Barrett's Esophagus. *Clin Gastroenterol Hepatol*. Nov 2022; 20(11): 2514-2523.e3. PMID 35183768
18. Ypsilantis E, Pissas D, Papagrigroriadis 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. PMID 24910941
19. 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): 539-47.e1. PMID 22749368
20. 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): 211-21. PMID 24219822

21. 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.* Sep 2011; 74(3): 465-72. PMID 21741642
22. Dunbar KB, Okolo P, 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.* Oct 2009; 70(4): 645-54. PMID 19559419
23. 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. PMID 30203202
24. 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): 907-13. PMID 24909555
25. 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): 967-74. PMID 26094505
26. Fuchs FS, Zirlik S, Hildner K, et al. Confocal laser endomicroscopy for diagnosing lung cancer in vivo. *Eur Respir J.* Jun 2013; 41(6): 1401-8. PMID 22997220
27. 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. PMID 32554957
28. Beji S, Wrist Lam G, stergren 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. PMID 33153363
29. Liem EIML, Freund JE, Savci-Heijink CD, et al. Validation of Confocal Laser Endomicroscopy Features of Bladder Cancer: The Next Step Towards Real-time Histologic Grading. *Eur Urol Focus.* Jan 15 2020; 6(1): 81-87. PMID 30033066
30. Nathan CA, Kaskas NM, Ma X, et al. Confocal Laser Endomicroscopy in the Detection of Head and Neck Precancerous Lesions. *Otolaryngol Head Neck Surg.* Jul 2014; 151(1): 73-80. PMID 24699456
31. 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): 632-7. PMID 26372409
32. Dittberner A, Ziadat R, Hoffmann F, et al. Fluorescein-Guided Panendoscopy for Head and Neck Cancer Using Handheld Probe-Based Confocal Laser Endomicroscopy: A Pilot Study. *Front Oncol.* 2021; 11: 671880. PMID 34195078
33. 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. PMID 24897112
34. 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.* 2015; 81(6): 1346-54. PMID 25680899
35. 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.* 2015; 49(5): 379-86. PMID 25485568
36. 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.* Jan 2019; 34(1): 84-91. PMID 30221400
37. 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(1): 109. PMID 27596838
38. 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): 366-76. PMID 27129127
39. 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. PMID 34012620
40. Kollar M, Krajciová J, Prefertusova L, et al. Probe-based confocal laser endomicroscopy versus biopsies in the diagnostics of oesophageal and gastric lesions: A prospective, pathologist-blinded study. *United European Gastroenterol J.* May 2020; 8(4): 436-443. PMID 32213027
41. Canakis A, Deliwala SS, Kadiyala J, et al. The diagnostic performance of probe-based confocal laser endomicroscopy in the detection of gastric cancer: a systematic review and meta-analysis. *Ann Gastroenterol.* 2022; 35(5): 496-502. PMID 36061161
42. 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. PMID 32282543
43. 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. PMID 31220640
44. 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.* 2020; 9(3): 180-186. PMID 32584313
45. 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. PMID 32433791
46. Kovacevic B, Antonelli G, Klausen P, et al. EUS-guided biopsy versus confocal laser endomicroscopy in patients with pancreatic cystic lesions: A systematic review and meta-analysis. *Endosc Ultrasound.* 2021; 10(4): 270-279. PMID 34290168
47. Konjeti VR, McCarty TR, Rustagi T. Needle-based Confocal Laser Endomicroscopy (nCLE) for Evaluation of Pancreatic Cystic Lesions: A Systematic Review and Meta-analysis. *J Clin Gastroenterol.* Jan 01 2022; 56(1): 72-80. PMID 33252557
48. De Palma GD, Esposito D, Luglio G, et al. Confocal laser endomicroscopy in breast surgery: a pilot study. *BMC Cancer.* Apr 10 2015; 15: 252. PMID 25885686
49. 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): 282-90. PMID 25616752



50. Martnek J, Kollr M, Krajčov 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. PMID 32736480
51. 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. PMID 33798541
52. Mi J, Han X, Wang R, et al. Diagnostic accuracy of probe-based confocal laser endomicroscopy and tissue sampling by endoscopic retrograde cholangiopancreatography in indeterminate biliary strictures: a meta-analysis. *Sci Rep.* May 04 2022; 12(1): 7257. PMID 35508585
53. 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): 570-80. PMID 16564854
54. 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.* Dec 2012; 76(6): 1087-94. PMID 23164510
55. Chandrasekhara V, Chathadi KV, Acosta RD, et al. The role of endoscopy in benign pancreatic disease. *Gastrointest Endosc.* Aug 2015; 82(2): 203-14. PMID 26077456
56. Muthusamy VR, Chandrasekhara V, Acosta RD, et al. The role of endoscopy in the diagnosis and treatment of cystic pancreatic neoplasms. *Gastrointest Endosc.* Jul 2016; 84(1): 1-9. PMID 27206409
57. Wani S, Rubenstein JH, Vieth M, et al. Diagnosis and Management of Low-Grade Dysplasia in Barrett's Esophagus: Expert Review From the Clinical Practice Updates Committee of the American Gastroenterological Association. *Gastroenterology.* Nov 2016; 151(5): 822-835. PMID 27702561
58. Muthusamy VR, Wani S, Gyawali CP, et al. AGA Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus: Expert Review. *Clin Gastroenterol Hepatol.* Dec 2022; 20(12): 2696-2706.e1. PMID 35788412
59. 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. PMID 34003218

## POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
March 2013	New policy	
March 2014	Replace policy	Policy updated with literature search. No change to policy statement. References 5, 6, 12, 16, 22, & 23 added; others renumbered or removed.
March 2015	Replace policy	Policy updated with literature review. Policy statement unchanged. References 12, 16-17, 22-23, and 28 added.
June 2016	Replace policy	Policy updated with literature review through October 7, 2015; references 20, 24, 26-27, 33-36, and 38 added. Policy statement unchanged.
March 2017	Replace policy	Policy updated with literature review; references 13 and 29-30 added. Policy statement changed from not medically necessary to investigational due to FDA 510(k) clearance.
March 2018	Replace policy	Policy updated with literature review through September 11, 2017; no references added. Policy statement unchanged.
March 2019	Replace policy	Policy updated with literature review through September 6, 2018; references 35-36 added. Policy statement unchanged.
March 2020	Replace policy	Policy updated with literature review through September 9, 2019; references added. Policy statement unchanged.
April 2021	Replace policy	Policy updated with literature review through October 1, 2020; references added. Policy statement unchanged.
December 2022	Replace policy	Policy updated with literature review through September 29, 2021; references added. Policy statement unchanged.
March 2023	Replace policy	Policy updated with literature review through October 17, 2022; references added. Policy statement unchanged.
March 2024	Replace policy	Policy updated with literature review through September 26, 2023; references added. Policy statement unchanged.

The policies contained in the FEP Medical Policy Manual are developed to assist in administering contractual benefits and do not constitute medical advice. They are not intended to replace or substitute for the independent medical judgment of a practitioner or other health care professional in the treatment of an individual member. The Blue Cross and Blue Shield Association does not intend by the FEP Medical Policy Manual, or by any particular medical policy, to recommend, advocate, encourage or discourage any particular medical technologies. Medical decisions relative to medical technologies are to be made strictly by members/patients in consultation with their health care providers. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that the Blue Cross and Blue Shield Service Benefit Plan covers (or pays for) this service or supply for a particular member.