

Chromoendoscopy as an Adjunct to Colonoscopy

Policy MP-037

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1. Policies are subject to change in accordance with State and Federal notice requirements.
2. Policies outline coverage determinations for U of U Health Plans Commercial, CHIP and Healthy U (Medicaid) plans. Refer to the "Policy" section for more information.
3. Services requiring prior-authorization may not be covered, if prior-authorization is not obtained.
4. **This Medical Policy does not guarantee coverage or payment of the service. The service must be a benefit in the member's plan and the member must be eligible for coverage at the time of service. Additional payment guidelines may be applied that are not included in this policy.**

Description:

Chromoendoscopy, also known as chromoscopy and chromocolonoscopy, refers to the application of topical stains or dyes during an endoscopic procedure. When used with colonoscopy, the intent is to increase the sensitivity of the procedure by facilitating the identification of mucosal abnormalities, particularly flat or depressed lesions. There are two types of chromoendoscopy; one involves actual spraying of dyes or stains through the working channel of an endoscope. The other type, known as virtual chromoendoscopy, uses a computer algorithm to simulate different colors of light that result from dye or stain spraying.

Chromoendoscopy can be used in the whole colon (pancolonic chromoendoscopy) on an untargeted basis or can be directed to a specific lesion or lesions (targeted chromoendoscopy). Surveillance for colorectal, esophageal, gastric or small bowel dysplasia as well as surveillance of dysplasia in high risk population such as those with inflammatory bowel disease are other usages.

The equipment used in regular chromoendoscopy is widely available however the pre-procedure setup is more in depth than routine endoscopy. For optimal use of chromoendoscopy, SURFACE guidelines have been developed to facilitate the use of chromoendoscopy during routine surveillance colonoscopy that include proper bowel preparation, the avoidance of active colitis, the use of an antispasmodic agent, and the ability to identify pit patterns. Optimal bowel preparation is especially necessary for adequate visualization during chromoendoscopy given that these pit patterns is used to guide targeted biopsies. Several review articles and technology assessments have indicated that, although the

techniques are simple, the procedure (e.g., the concentration of dye and amount of dye sprayed) is variable and the results dependent on the endoscopist's experience using chromoendoscopy, and thus classification of mucosal staining patterns for identifying specific conditions is not standardized and varies widely.

Indigo carmine, a contrast stain, is the most commonly used stain with colonoscopy to enhance the detection of colorectal neoplasms. Methylene blue, which stains the normal absorptive epithelium of the small intestine and colon, has been used to detect colonic neoplasia and to aid in the detection of intraepithelial neoplasia in patients with chronic ulcerative colitis. Also, crystal violet (also known as gentian violet) stains cell nuclei and has been applied in the colon to enhance visualization of pit patterns (i.e., superficial mucosal detail).

Policy Statement and Criteria

1. Commercial Plans/CHIP

U of U Health Plans does NOT cover chromoendoscopy and/or virtual chromoendoscopy as adjunct to diagnostic or screening colonoscopies as they are considered investigational.

2. Medicaid Plans

Coverage is determined by the State of Utah Medicaid program; if Utah State Medicaid has no published coverage position and InterQual criteria are not available, the U of U Health Plans Commercial criteria will apply. For the most up-to-date Medicaid policies and coverage, please visit their website at: <https://medicaid.utah.gov/utah-medicaid-official-publications/> or the [Utah Medicaid code Look-Up tool](#)

CPT/HCPCS codes covered by Utah State Medicaid may still require further evaluation to determine medical necessity for coverage.

Clinical Rationale

Studies identified, which assessed chromoendoscopy, include Kahi et al. who conducted a large randomized trial in 2010 to determine if using high-definition chromocolonoscopy in average-risk patients would increase the findings of flat depressed neoplasms. The authors evaluated 660 patients at 4 centers in the United States, who had an average risk of colorectal cancer (CRC), were aged ≥ 50 years, and were having their first screening colonoscopy. Participants were randomized to High-definition chromoendoscopy with indigo carmine dye (n=321) or to High-definition white-light colonoscopy (WLC) (n=339). The primary outcomes were compared between the groups by the proportion of patients with at least 1 adenoma and the mean number of adenomas per patient. No significant between-group differences were noted for either outcome. A total of 178 (55.5%) subjects in the chromoendoscopy group and 164 (48.4%) subjects in the standard colonoscopy group had 1 or more adenomas (p=0.07). The mean number of adenomas per subject, that were less than 5 mm in diameter, differed statistically significantly between groups (0.8 for chromoendoscopy vs 0.7 for standard endoscopy; p=0.03) though the clinical meaningfulness of this difference is questionable. The difference between groups in the mean number of adenomas 10 mm or larger was not statistically significant (0.11 for chromoendoscopy vs 0.12 for standard colonoscopy; p=0.70). Thirty-nine (12%) subjects in the chromoendoscopy group

and 49 (15%) subjects in the standard colonoscopy group had 3 or more adenomas; the difference between groups was not statistically significant ($p=0.40$). The authors found chromocolonoscopy marginally increased detection overall for adenomas; including flat and small adenomas over WLC. The findings of advanced neoplasms were similar between the two methods. The high adenoma detection rate could have been due to the use of high-definition technology used in both groups; therefore the use of chromocolonoscopy in average-risk patients is not recommended for CRC screening.

A 2012 pilot study (Kiriya et al.) assessed the utility of using computed virtual chromoendoscopy with the flexible spectral imaging color enhancement (FICE) for colon neoplasia screening. One hundred consecutive patients (2 were excluded because insertion was not possible) referred for a colonoscopy following a sigmoidoscopy or for postoperative surveillance after anterior resection; received virtual chromoendoscopy using FICE or white-light colonoscopy (WLC) in random order. All lesions (a total of 110) were identified and removed during either examination and evaluated. Of these, 65 lesions were detected using FICE and 45 with WLC; the difference in the number of detected lesions did not differ significantly between groups. Most lesions detected were neoplastic; of these, 59 (91%) were found using FICE and 38 (84%) using WLC. The miss rate for all polyps with FICE (12/39 [31%] lesions) was significantly lower than with WLC (28/61 [46%] lesions; $p=0.03$). Twenty-six (44%) of 59 neoplastic lesions detected by FICE and 14 (37%) of 38 of neoplastic lesions detected by WLC were at least 5 mm in size. There was no statistically significant difference between the 2 procedures in terms of the number of lesions larger than 5 mm detected. In conclusion, under proper bowel preparation, colonoscopy using FICE may enhance the detection of flat and/or diminutive adenomatous lesions compared with WLC.

Wanders et al. evaluated 3 types of endoscopic technologies, in this 2013 meta-analysis, to see if any of them could allow optical diagnosis and resection of colonic polyps without histopathological testing. The authors analyzed the sensitivity, specificity, and real-time negative predictive value of narrowed spectrum endoscopy (narrow-band imaging (NBI), image-enhanced endoscopy [i-scan], Fujinon intelligent chromoendoscopy [FICE]), confocal laser endomicroscopy (CLE), and auto-fluorescence imaging for differentiation between neoplastic and non-neoplastic colonic lesions. The authors concluded that all endoscopic imaging techniques other than auto-fluorescence imaging could be used if the endoscopists are appropriately trained to make a reliable optical diagnosis for colonic lesions in daily practice. However, further research is needed focusing on whether training could help to improve negative predictive values.

In a 2014 randomized trial, Freire et al. analyzed 145 patients (17 were excluded for poor bowel preparation) with longstanding (at least 8 years) distal/extensive ulcerative colitis without primary sclerosing cholangitis and/or a history of intra-epithelial neoplasia that were clinically inactive. Patients were prospectively randomized to undergo conventional colonoscopy or colonoscopy with chromoendoscopy (using methylene blue). A total of 104 lesions were identified in the chromoendoscopy group, and 63 were identified in the conventional colonoscopy group. The primary study outcome (number of low grade intraepithelial neoplasias detected) did not differ significantly between groups (7 with chromoendoscopy vs 6 with conventional colonoscopy). Compared with standard histologic evaluation, the sensitivity and specificity of chromoendoscopy for detecting intraepithelial neoplasia were 85.7% and 97.9%, respectively. The study concluded, chromoendoscopy takes longer and does not improve the detection of intraepithelial neoplasia in the endoscopic screening of patients with ulcerative colitis.

A 2015 large retrospective study (Mooiweer et al.) examined data on 937 patients for the detection of dysplasia in patients with inflammatory bowel disease (IBD), from 3 referral centers, who had undergone surveillance from Jan 2000 through November 2013 and had a diagnosis of ulcerative colitis or Crohn disease. The detection of neoplasia detection was evaluated between chromoendoscopy (440

procedures in 401 patients) and white-light colonoscopy (WLC) (1802 procedures in 772 patients). Neoplasia was detected in 48 (11%) of 440 colonoscopies performed with chromoendoscopy (95% CI, 8% to 14%) and in 189 (10%) of 1802 procedures performed with WLC (95% CI, 9% to 12%). Targeted biopsies yielded 59 dysplastic lesions in the chromoendoscopy group, comparable to the 211 dysplastic lesions detected in the WLC group (P=0.30). The study concluded that implementation of chromoendoscopy for IBD surveillance did not increase dysplasia detection compared with WLC for targeted and random biopsies.

In a 2016 retrospective cohort study, Gasia et al. evaluated data from 454 patients with IBD who had undergone surveillance for at least 8 years, at a single tertiary care center. The physicians chose which endoscopic approach they wanted to use between high-definition colonoscopy, chromoendoscopy, and virtual chromoendoscopy; although only one of the 8 endoscopists had training in chromoendoscopy. A total of 126 patients had a standard colonoscopy, 182 had a high-definition colonoscopy (124 with random biopsies, 58 with targeted biopsies), 28 had chromoendoscopy (4 with random biopsies, 24 with targeted biopsies), and 118 had virtual chromoendoscopy (64 with random biopsy, 54 with targeted biopsies). Rates of neoplasia detection were significantly higher in the targeted biopsy groups (19.1%; 95% CI, 13.4% to 26.5%) than in the random biopsy groups (8.2%; 95% CI, 5.6% to 11.7%). However, there were no significant differences in neoplasia detection rates with targeted biopsy throughout any of the endoscopic approaches that were used within the groups.

UpToDate (Canto) reviewed chromoendoscopy as an adjunct to colonoscopy in 2025 and found that, given the mixed results with regard to the effectiveness of chromoendoscopy for adenoma detection and the increased time required to perform the procedure, the use of chromoendoscopy for the routine detection of colorectal neoplasia needs to be individualized.

UpToDate (Shergill et al) performed a literature review current through February 2025 on chromoendoscopy and surveillance of dysplasia in patients with inflammatory bowel disease (IBD). Those studies found some limitations to chromoendoscopy such as it can be time consuming, providers are not trained appropriately in using this technology, and there is lack in the standardization for classifications of the findings; which may contribute to misinterpretations of results. There are limited studies on the impact of patient's outcomes and some studies found that chromoendoscopy increases adenoma detection rates in the colon, while other have not. Some experts caution the use of chromoendoscopy for surveillance until further studies have demonstrated the efficacy in clinical practice or its long term benefit. In conclusion, screening colonoscopies continue to be the best tool to detect dysplasia and colorectal cancer in patients with IBD.

Some specialty society's support for chromoendoscopy has evolved despite the limited evidence supporting its impact on health outcomes. In 2014, the European Society of Gastrointestinal Endoscopy (ESGE) issued guidelines on advanced endoscopic imaging (i.e. chromoendoscopy) for the detection and differentiation of colorectal neoplasia in which it suggested the use of advanced endoscopic imaging for margin assessment and prediction of deep submucosal invasion in lesions with a depressed component or non-granular or mixed-type laterally spreading tumors (LSTs). Even though the quality of evidence supporting these recommendations was considered very low and moderate for margin delineation and assessment of depth of submucosal invasion. Since 2017 there has been no new evidence with clinically relevant endpoints for the patients (incomplete resection, interrupted procedure, cancer detection) published to further support its use. The authors concluded, "The availability, feasibility, and minimum standard of advanced imaging use, particularly in the community setting, are unknown. Colonoscopy services should set up structured monitoring and initiate audit to generate further evidence for advanced imaging."

The European Society of Gastrointestinal Endoscopy (ESGE) Guidelines of 2016 address the utilization of advanced endoscopic imaging in gastrointestinal (GI) endoscopy. The ESGE suggests:

1. Advanced endoscopic imaging technologies may improve mucosal visualization and enhance fine structural and microvascular detail; however, only low quality of evidence was found. "Expert endoscopic diagnosis may be improved by advanced imaging, but as yet in community-based practice no technology has been shown consistently to be diagnostically superior to current practice with high definition white light."
2. The use of validated classification systems to support the use of optical diagnosis with advanced endoscopic imaging in the upper and lower GI tracts; although only moderate quality of evidence was found.
3. Training may improve performance in the use of advanced endoscopic imaging techniques and should be a prerequisite for use in clinical practice. A learning curve exists and training alone does not guarantee sustained high performances in clinical practice.

The ESGE concluded that "advanced endoscopic imaging can improve mucosal visualization and endoscopic diagnosis; however it requires training and the use of validated classification systems."

The 2015 consensus statement approved by the American Gastroenterology Association (AGA) and the American Society of Gastrointestinal Endoscopy (ASGE) regarding Surveillance for Colorectal Endoscopic Neoplasia Detection and Management in Inflammatory Bowel Disease Patients: International Consensus Recommendations (SCENIC) was that although chromoendoscopy is a promising surveillance tool for inflammatory bowel disease patients, larger trials of chromoendoscopy using high-definition colonoscopy is needed and at this time, it can only be suggested over the use of white-light colonoscopy.

The National Comprehensive Cancer Network (NCCN) guidelines for Genetic/Familial High-Risk Assessment: Colorectal version 3.2024 states that "chromoendoscopy may be considered in patients with Lynch syndrome, but larger prospective randomized trials are needed to better understand its role in Lynch syndrome."

In conclusion, although chromoendoscopy has been shown to be beneficial in patients with a high risk of dysplasia such as IBD patients, the ASGE and the AGA do not universally recommend or endorse the broad use of chromoendoscopy at this time except in IBD patients where this technology can be considered as an alternative to standard colonoscopy as is detailed in the SCENIC consensus. The American College of Gastroenterology (ACG) has also stated that chromocolonoscopy with targeted biopsies could be done by a trained endoscopist instead of random biopsies used during routine white-light colonoscopy and could be useful in IBD patients who are at a high risk of cancer (such as those with a history of dysplasia), however not in low risk IBD patients. A significant limitation of all studies that is recognized by the AGA, ASGE and ACG is that the results of these procedures are operational dependent and are limited by the experience of the endoscopist and likely accounts for the variability in the results. Although the results are promising, the results of chromoendoscopy have not been found to be universally accurate and therefore cannot be broadly implemented at this time. The cost of the equipment and adequate training at this time continue to be important concerns and must be addressed before this technology is part of the standard of care for community gastroenterologists.

Applicable Coding

CPT Codes

44799 Unlisted procedure, small intestine

45399 Unlisted procedure, colon

HCPCS Codes

No applicable codes

References:

1. Bhagya Rao B, Bhattacharya A, Lichtenstein GR. Precision Medicine: Predicting Disease Course in Patients with Inflammatory Bowel Disease. *Current Treatment Options in Gastroenterology*. 2020 Dec;18:574-88.
2. Buchner, A. M. (2017). "The Role of Chromoendoscopy in Evaluating Colorectal Dysplasia." *Gastroenterol Hepatol (N Y)* 13(6): 336-347.
3. Canto, MI, M. "Chromoendoscopy". UpToDate. Topic 2670 Version 27.0. Literature review current through February 2025. Last topic updated January 27, 2025. Available at: https://www.uptodate.com/contents/chromoendoscopy?search=chromoendoscopy&source=search_result&selectedTitle=1~97&usage_type=default&display_rank=1
4. Flynn AD, Valentine JF. Chromoendoscopy for Dysplasia Surveillance in Inflammatory Bowel Disease. *Inflamm Bowel Dis*. 2018 Jun 8;24(7):1440-1452. doi: 10.1093/ibd/izy043. PMID: 29668929.
5. Freire P, Figueiredo P, Cardoso R, et al. Surveillance in ulcerative colitis: is chromoendoscopy-guided endomicroscopy always better than conventional colonoscopy? A randomized trial. *Inflamm Bowel Dis*. Nov 2014;20(11):2038-2045. PMID 25185683
6. Gasia MF, Ghosh S, Panaccione R, et al. Targeted biopsies identify larger proportions of patients with colonic neoplasia undergoing high-definition colonoscopy, dye chromoendoscopy, or electronic virtual chromoendoscopy. *Clin Gastroenterol Hepatol*. May 2016;14(5):704-712 e704. PMID 26804384
7. Hayes, Inc. (2018) "Chromoendoscopy for Colonoscopy". Search and Summary. September 28, 2018. Available at: <https://www.hayesinc.com/subscribers/displaySubscriberArticle.do?articleId=92846> – Archived-no longer available
8. Kahi CJ, Anderson JC, Waxman I, et al. High-definition chromocolonoscopy vs. high-definition white light colonoscopy for average-risk colorectal cancer screening. *Am J Gastroenterol*. Jun 2010;105(6):1301-1307. PMID 20179689
9. Kaminski MF, Hassan C, Bisschops R, et al. Advanced imaging for detection and differentiation of colorectal neoplasia: European Society of Gastrointestinal Endoscopy (ESGE) Guideline. *Endoscopy* 2014; 46: 435-457 Available at: <http://www.esge.com/performance-measures-for-lower-gastrointestinal-endoscopy.html>
10. Kiesslich, R. (2022). "Colour me blue: chromoendoscopy and advanced detection methods in ulcerative colitis." *Curr Opin Gastroenterol* 38(1): 67-71.
11. Kiriya S, Matsuda T, Nakajima T, et al. Detectability of colon polyp using computed virtual chromoendoscopy with flexible spectral imaging color enhancement. *Diagn Ther Endosc*. Apr 2012;2012:596303. PMID 22474404
12. Laine, L., et al. (2015). "SCENIC international consensus statement on surveillance and management of dysplasia in inflammatory bowel disease." *Gastroenterology* 148(3): 639-651 e628.
13. Lichtenstein GR. (2022) "Emerging Treatments for Inflammatory Bowel Disease. *Gastroenterology & Hepatology*". 2022 Aug;18(8):437.
14. Lichtenstein, G. R. (2018). "Highlights From the New ACG Guideline on Crohn's Disease Management." *Gastroenterol Hepatol (N Y)* 14(8): 482-484.
15. Lichtenstein GR. (2022) "Spotlight on Inflammatory Bowel Disease. *Gastroenterology & Hepatology*". 2022 Jan;18(1):7.
16. Mooiweer E, van der Meulen-de Jong AE, Ponsioen CY, et al. Chromoendoscopy for surveillance in inflammatory bowel disease does not increase neoplasia detection compared with conventional colonoscopy with random biopsies: results from a large retrospective study. *Am J Gastroenterol*. Jul 2015;110(7):1014-1021. PMID 25823770
17. Resende RH, Ribeiro IB, de Moura DT, Galetti F, de Paula Rocha RS, Bernardo WM, Sakai P, de Moura EG. Surveillance in inflammatory bowel disease: is chromoendoscopy the only way to go? A systematic review and meta-analysis of randomized clinical trials. *Endoscopy international open*. 2020 May;8(05):E578-90.
18. Shergill, A, MD. Odze, R, MD. Farraye, F, MD. "Surveillance and management of dysplasia in patients with inflammatory bowel disease" UpToDate. Topic 4079 Version 40.0. Literature review current through February 2025. Topic last updated: March 7, 2025. Available at: https://www.uptodate.com/contents/surveillance-and-management-of-dysplasia-in-patients-with-inflammatory-bowel-disease?search=Surveillance%20and%20management%20of%20dysplasia%20in%20patients%20with%20inflammatory%20bowel%20disease&source=search_result&selectedTitle=1%7E150&usage_type=default&display_rank=1

19. Singh R, Chiam KH, Leiria F, Pu LZCT, Choi KC, Militz M. Chromoendoscopy: role in modern endoscopic imaging. *Transl Gastroenterol Hepatol*. 2020 Jul 5;5:39. doi: 10.21037/tgh.2019.12.06. PMID: 32632390; PMCID: PMC7063532.
20. The National Comprehensive Cancer Network (NCCN) guidelines. "Genetic/Familial High-Risk Assessment: Colorectal" Version 3.2024. Accessed: March 12, 2025. Available at: <https://www.nccn.org/guidelines/guidelines-detail?category=2&id=1544>
21. 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):1337-1347.
22. Wijnands AM, Mahmoud R, Lutgens MW, Oldenburg B. Surveillance and management of colorectal dysplasia and cancer in inflammatory bowel disease: Current practice and future perspectives. *European Journal of Internal Medicine*. 2021 Nov 1;93:35-41.
23. Wilson, A, Bisschops, R, Roelandt, P., et al. (2016) European Society of Gastrointestinal Endoscopy (ESGE) Guideline. "Advanced endoscopic imaging: European Society of Gastrointestinal Endoscopy (ESGE) Technology Review". Available at: <https://eref.thieme.de/cockpits/clGuidelinesEndoscopy0001/12972122120401859266/coEGuideline00001/4-45>

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