Corporate Medical Policy

Chromoendoscopy as an Adjunct to Colonoscopy

File Name: chromoendoscopy_as_an_adjunct_to_colonoscopy
Origination: 7/2012
Last Review: 11/2024

Description of Procedure or Service

Chromoendoscopy refers to the application of dyes or stains during endoscopy to enhance tissue differentiation or characterization. When used with colonoscopy, the intent is to increase the sensitivity of the procedure by facilitating the identification of mucosal abnormalities. 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.

Background

Colonoscopy, a procedure during which colonic and rectal polyps can be identified and removed, is considered the criterion standard test for colorectal cancer screening and diagnosis of colorectal disease. However, colonoscopy is an imperfect procedure. A recent systematic review and meta-analysis by Zhao et al (2019) pooled findings from more than 15,000 tandem (i.e. back-to-back) colonoscopy studies in 43 publications and found a miss rate of 26% for adenomas, 9% for advanced adenomas, and 27% for serrated polyps. Miss rates were higher for proximal advanced adenomas (14%), serrated polyps (27%), flat adenomas (34%), and in patients at high risk for CC (33%).

Several adjunct endoscopic techniques, including chromoendoscopy, could potentially enhance the sensitivity of colonoscopy. Chromoendoscopy, also known as chromoscopy and chromocolonoscopy, refers to the application of topical stains or dyes during endoscopy in order to enhance tissue differentiation or characterization and facilitate the identification of mucosal abnormalities. Chromoendoscopy may be particularly useful for detecting flat or depressed lesions. Standard colonoscopy uses white light to view the colon. In chromoendoscopy, stains are applied, resulting in color highlighting of areas of surface morphology of epithelial tissue. The dyes or stains are applied via a spray catheter that is inserted down the working channel of the endoscope. 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). Chromoendoscopy differs from endoscopic tattooing in that the former uses transient stains, whereas tattooing involves the use of a long-lasting pigment for future localization of lesions.

Stains and dyes used in chromoendoscopy can be placed in the following categories:

- Absorptive: These stains are preferentially absorbed by certain types of epithelial cells.
- Contrast: These stains seep through mucosal crevices and highlight surface topography.
- Reactive: These stains undergo chemical reactions when in contact with specific cellular constituents, which results in a color change.

Reactive stains are primarily used to identify gastric abnormalities and are not used with colonoscopy. Indigo carmine, a contrast stain, is one of the most commonly used stains with colonoscopy to enhance the detection of colorectal neoplasms. Several absorptive stains are also used with colonoscopy. Methylene blue is widely used; it stains the normal absorptive epithelium of the small intestine and colon and has been used to detect colonic neoplasia and to aid in the detection of intraepithelial neoplasia in individuals with chronic ulcerative colitis. In addition, 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).

Potential applications of chromoendoscopy as an alternative to standard colonoscopy include:

- Diagnosis of colorectal neoplasia in symptomatic individuals at increased risk of colorectal cancer due to family history of colorectal cancer, personal history of adenomas, etc.
- Identification of mucosal abnormalities for targeted biopsy as an alternative to multiple random biopsies in individuals with inflammatory bowel disease (IBD)
- Screening the general population for colorectal cancer

The equipment used in regular chromoendoscopy is widely available. Several authors of review articles and technology assessments have stated that, although the techniques are simple, the procedure, e.g. concentration of dye and amount of dye sprayed, is variable and classification of mucosal staining patterns for identifying specific conditions is not standardized.

Virtual chromoendoscopy (also called electronic chromoendoscopy) involves imaging enhancements with endoscopy systems that could potentially be an alternative to dye spraying. One system is the Fujinon Intelligent Color Enhancement feature (Fujinon, Inc.). This technology uses post-processing computer algorithms to modify the light reflected from the mucosa from conventional white light to various other wavelengths.

Regulatory Status

In 2014, the Fujifilm EPX-4440HD Digital Video Processor with Fujinon Intelligent Color Enhancement (FICE®) and Light Source (FujiFilm) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. FDA documents state that FICE® can be used to supplement white-light endoscopy but is not intended to replace histopathologic sampling as a means of diagnosis.

In 2012, i-SCAN™ (Pentax), used for virtual chromoendoscopy, was cleared for marketing by FDA through the 510(k) process. This is a digital image enhancement technology is part of the Pentax EPK-i5010 Video Processor. The i-SCAN™ has several modes that digitally enhance images in real–time during endoscopy. FDA documents state that i-SCAN™ is intended as an adjunct following white-light endoscopy and is not intended to replace histopathologic analysis.

No dye or stain product has been specifically approved by the FDA for use in chromoendoscopy.

Related Policies:
Confocal Laser Endomicroscopy

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

Chromoendoscopy and virtual chromoendoscopy are considered investigational as an adjunct to diagnostic or surveillance colonoscopy. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit

design; therefore, member benefit language should be reviewed before applying the terms of this medical policy.

When Chromoendoscopy as an Adjunct to Colonoscopy is covered

Not applicable.

When Chromoendoscopy as an Adjunct to Colonoscopy is not covered

Chromoendoscopy and virtual chromoendoscopy are considered investigational as an adjunct to diagnostic or surveillance colonoscopy.

Policy Guidelines

The evidence for chromoendoscopy in patients who have an average risk of colorectal cancer (CC) undergoing colonoscopy includes randomized controlled trials (RCTs) and a meta-analysis of these RCTs. Relevant outcomes are overall survival (OS), disease-specific survival (DSS), test validity, and change in disease status. The meta-analysis demonstrated that dye-based chromoendoscopy increased the adenoma detection rate and adenomas per colonoscopy in patients at average or increased risk of CC compared to standard or high-definition white light colonoscopy. However, limitations included unclear indication of colonoscopy in the studies (which included patients with screening and surveillance), and some heterogeneity in mean adenomas per patient. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

The evidence for chromoendoscopy in patients who have an increased risk of CC undergoing colonoscopy includes multiple RCTs and systematic reviews. Relevant outcomes are OS, DSS, test validity, and change in disease status. A Cochrane systematic review of trials comparing chromoendoscopy with standard colonoscopy in high-risk patients (but excluding those with inflammatory bowel disease [IBD]) found significantly higher rates of adenoma detection and rates of 3 or more adenomas with chromoendoscopy compared with standard colonoscopy. The evidence for detecting larger polyps, defined as greater than 5 mm or greater than 10 mm, is less robust. While 1 study reported a significantly higher detection rate for polyps greater than 5 mm, no studies reported increased detection of polyps greater than 10 mm. A recent RCT and systematic review involving patients with Lynch syndrome also found equivocal results. Results from the RCT showed similar neoplasia detection rates with chromoendoscopy and conventional white-light colonoscopy, while the systematic review concluded that chromoendoscopy is associated with significantly improved detection of certain lesions; however, the odds of having an adenoma detected were not significantly different between the modalities. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

The evidence for chromoendoscopy in patients who have inflammatory bowel disease undergoing colonoscopy includes meta-analyses and RCTs. Relevant outcomes are OS, DSS, test validity, and change in disease status. Several meta-analyses found a statistically significant higher yield of chromoendoscopy over standard white-light colonoscopy for detecting dysplasia. The evidence supported improved polyp detection rates, with chromoendoscopy; however, the studies had limitations such as lack of information regarding the timing of the screening modalities. A recent RCT found increased detection of dysplasia with chromoendoscopy compared to white-light endoscopy, although the benefit was only observed in a subgroup analysis in the second half of the study follow-up period. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have an average risk of CC who receive virtual chromoendoscopy, the evidence includes several RCTs and systematic reviews with meta-analyses. Relevant outcomes are OS, DSS, test validity, and change in disease status. The available RCTs have not found that virtual chromoendoscopy improves the detection of clinically important polyps compared with standard

white-light colonoscopy. Moreover, there is a lack of studies assessing the impact of virtual chromoendoscopy on CC incidence and mortality rates compared with standard colonoscopy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have an increased risk of CC who receive virtual chromoendoscopy, the evidence includes RCTs. Relevant outcomes are OS, DSS, test validity, and change in disease status. The available RCTs have not found that virtual chromoendoscopy improves the detection of clinically important polyps compared with standard white-light colonoscopy. Moreover, there is a lack of studies assessing the impact of virtual chromoendoscopy on CC incidence and mortality rates compared with standard colonoscopy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have IBD who receive virtual chromoendoscopy, the evidence includes 2 meta-analyses and 2 RCTs. Relevant outcomes are OS, DSS, test validity, and change in disease status. One meta-analysis showed superiority of virtual chromoendoscopy over high-definition white light colonoscopy for dysplasia per biopsy and ranked virtual chromoendoscopy as the best option for screening among the different modalities in comparison. The second meta-analysis found no difference between dye-based chromoendoscopy and virtual chromoendoscopy for dysplasia detection. One RCT found a significantly greater likelihood that virtual chromoendoscopy would correctly identify the extent of disease inflammation than standard colonoscopy but no significant difference in the likelihood of identifying disease activity. The other RCT found that there was no significant difference in the detection of neoplasia between high-definition white light versus high-definition virtual chromoendoscopy in patients with long-standing IBD. There is a lack of studies assessing the impact of virtual chromoendoscopy on CC incidence and mortality rates compared with standard colonoscopy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *No specific code.*

There is no specific code for chromoendoscopy. The additional work of the chromoendoscopy would probably be reported with the unlisted CPT code 44799.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.84, 3/8/12

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.84, 3/14/13

Specialty Matched Consultant Advisory Panel 10/2013

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.84, 3/13/14

Specialty Matched Consultant Advisory Panel 11/2014

Senior Medical Director review 12/2014

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.84, 3/12/15

Specialty Matched Consultant Advisory Panel 11/2015

Medical Director review 11/2015

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.84, 11/12/15

Specialty Matched Consultant Advisory Panel 11/2016

Medical Director review 11/2016

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.84, 11/2016

Specialty Matched Consultant Advisory Panel 11/2017

Medical Director review 11/2017

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.84, 11/2017

Specialty Matched Consultant Advisory Panel 11/2018

Medical Director review 11/2018

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.84, 11/2018

Specialty Matched Consultant Advisory Panel 11/2019

Medical Director review 11/2019

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.84, 11/2019

Specialty Matched Consultant Advisory Panel 11/2020

Medical Director review 11/2020

BCBSA Medical Policy Reference Manual [Electronic Version]. 2.01.84, 12/2020

Specialty Matched Consultant Advisory Panel 11/2021

Medical Director review 11/2021

Specialty Matched Consultant Advisory Panel 11/2022

Medical Director review 11/2022

Zhao S, Wang S, Pan P, et al. Magnitude, Risk Factors, and Factors Associated with Adenoma Miss Rate of Tandem Colonoscopy: A Systematic Review and Meta-analysis. Gastroenterology. May 2019; 156(6): 1661-1674.e11. PMID 30738046

U.S. Food & Drug Administration. 510(k) Premarket Notification (K140149). 2014; https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm?ID=K140149

Food and Drug Administration (FDA). 510(k) Summary: Pentax EPK-i5010 Video Processor. 2013; http://www.accessdata.fda.gov/cdrh_docs/pdf12/K122470.pdf

Antonelli G, Correale L, Spadaccini M, et al. Dye-based chromoendoscopy for the detection of colorectal neoplasia: meta-analysis of randomized controlled trials. Gastrointest Endosc. Sep 2022; 96(3): 411-422. PMID 35588768

Har-Noy O, Yung DE, Koulaouzidis A, et al. Chromoendoscopy or white light endoscopy for neoplasia detection in Lynch syndrome, a meta-analysis. Dig Liver Dis. Nov 2019; 51(11): 1515-1521. PMID 31526715

Brown SR, Baraza W. Chromoscopy versus conventional endoscopy for the detection of polyps in the colon and rectum. Cochrane Database Syst Rev. Oct 06, 2010; (10): CD006439. PMID 20927746

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Medical Director review 11/2023

Pohl J, Schneider A, Vogell H, et al. Pancolonic chromoendoscopy with indigo carmine versus standard colonoscopy for detection of neoplastic lesions: a randomised two-centre trial. Gut. Apr 2011; 60(4): 485-90. PMID 21159889

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): 1301-7. PMID 20179689

Resende RH, Ribeiro IB, de Moura DTH, et al. Surveillance in inflammatory bowel disease: is chromoendoscopy the only way to go? A systematic review and meta-analysis of randomized clinical trials. Endosc Int Open. May 2020; 8(5): E578-E590. PMID 32355874

Gondal B, Haider H, Komaki Y, et al. Efficacy of various endoscopic modalities in detecting dysplasia in ulcerative colitis: A systematic review and network meta-analysis. World J Gastrointest Endosc. May 16, 2020; 12(5): 159-171. PMID 32477450

Feuerstein JD, Rakowsky S, Sattler L, et al. Meta-analysis of dye-based chromoendoscopy compared with standard- and high-definition white-light endoscopy in patients with inflammatory bowel disease at increased risk of colon cancer. Gastrointest Endosc. Aug 2019; 90(2): 186-195.e1. PMID 31009609

Le Rhun M, Coron E, Parlier D, et al. High-resolution colonoscopy with chromoscopy versus standard colonoscopy for the detection of colonic neoplasia: a randomized study. Clin Gastroenterol Hepatol. Mar 2006; 4(3): 349-54. PMID 16527699

Stoffel EM, Turgeon DK, Stockwell DH, et al. Chromoendoscopy detects more adenomas than colonoscopy using intensive inspection without dye spraying. Cancer Prev Res (Phila). Dec 2008; 1(7): 507-13. PMID 19139000

Brown SR, Baraza W, Din S, et al. Chromoscopy versus conventional endoscopy for the detection of polyps in the colon and rectum. Cochrane Database Syst Rev. Apr 07, 2016; 4(4): CD006439. PMID 27056645

Desai M, Viswanathan L, Gupta N, et al. Impact of Electronic Chromoendoscopy on Adenoma Miss Rates During Colonoscopy: A Systematic Review and Meta-analysis. Dis Colon Rectum. Sep 2019; 62(9): 1124-1134. PMID 31162375

Omata F, Ohde S, Deshpande GA, et al. Image-enhanced, chromo, and cap-assisted colonoscopy for improving adenoma/neoplasia detection rate: a systematic review and meta-analysis. Scand J Gastroenterol. Feb 2014; 49(2): 222-37. PMID 24328858

Chung SJ, Kim D, Song JH, et al. Comparison of detection and miss rates of narrow band imaging, flexible spectral imaging chromoendoscopy and white light at screening colonoscopy: a randomised controlled back-to-back study. Gut. May 2014; 63(5): 785-91. PMID 23853211

Chung SJ, Kim D, Song JH, et al. Efficacy of computed virtual chromoendoscopy on colorectal cancer screening: a prospective, randomized, back-to-back trial of Fuji Intelligent Color Enhancement versus conventional colonoscopy to compare adenoma miss rates. Gastrointest Endosc. Jul 2010; 72(1): 136-42. PMID 20493487

Pohl J, Lotterer E, Balzer C, et al. Computed virtual chromoendoscopy versus standard colonoscopy with targeted indigocarmine chromoscopy: a randomised multicentre trial. Gut. Jan 2009; 58(1): 73-8. PMID 18838485

Kiriyama S, Matsuda T, Nakajima T, et al. Detectability of colon polyp using computed virtual chromoendoscopy with flexible spectral imaging color enhancement. Diagn Ther Endosc. 2012; 2012: 596303. PMID 22474404

Cha JM, Lee JI, Joo KR, et al. A prospective randomized study on computed virtual chromoendoscopy versus conventional colonoscopy for the detection of small colorectal adenomas. Dig Dis Sci. Aug 2010; 55(8): 2357-64. PMID 19834809

Neumann H, Vieth M, Günther C, et al. Virtual chromoendoscopy for prediction of severity and disease extent in patients with inflammatory bowel disease: a randomized controlled study. Inflamm Bowel Dis. Aug 2013; 19(9): 1935-42. PMID 23839228

Kandiah K, Subramaniam S, Thayalasekaran S, et al. Multicentre randomised controlled trial on virtual chromoendoscopy in the detection of neoplasia during colitis surveillance high-definition colonoscopy (the VIRTUOSO trial). Gut. Sep 2021; 70(9): 1684-1690. PMID 33214162

Alexandersson B, Hamad Y, Andreasson A, et al. High-Definition Chromoendoscopy Superior to High-Definition White-Light Endoscopy in Surveillance of Inflammatory Bowel Diseases in a Randomized Trial. Clin Gastroenterol Hepatol. Aug 2020; 18(9): 2101-2107. PMID 32353535

Wan J, Zhang Q, Liang SH, et al. Chromoendoscopy with targeted biopsies is superior to white-light endoscopy for the long-term follow-up detection of dysplasia in ulcerative colitis patients: a multicenter randomized-controlled trial. Gastroenterol Rep (Oxf). Jan 2021; 9(1): 14-21. PMID 33747522

Yang DH, Park SJ, Kim HS, et al. High-Definition Chromoendoscopy Versus High-Definition White Light Colonoscopy for Neoplasia Surveillance in Ulcerative Colitis: A Randomized Controlled Trial. Am J Gastroenterol. Oct 2019; 114(10): 1642-1648. PMID 31567166

Mohammed N, Kant P, Abid F et al. OC-028 High-definition white light endoscopy (HDWLE) versus high definition with chromoendoscopy (HDCE) in the detection of dysplasia in long standing ulcerative colitis: a randomised controlled trial. Gut 2015.

Hussain MR, Ali FS, Tangri A, et al. The incremental yield of adenoma detection with I-Scan versus high-definition white light colonoscopy-a systematic review and meta-analysis of randomized studies. Int J Colorectal Dis. Sep 27, 2023; 38(1): 240. PMID 37755588

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Policy Implementation/Update Information

07/24/12 New policy issued. Chromoendoscopy and virtual chromoendoscopy are considered investigational as an adjunct to diagnostic or surveillance colonoscopy. Notification given 7/24/12 for policy effective date of 10/30/12. (sk)

5/28/13 Related policy added. Reference added. No change to policy statement. (sk)

11/12/13 Specialty Matched Consultant Advisory Panel review 10/16/2013. No change to policy statement. (sk)

5/27/14 Reference added. No change to Policy statement. (sk)

1/13/15 References update. Specialty Matched Consultant Advisory Panel review 11/2014. Senior Medical Director review 12/2014. No change to Policy statement. (td)

4/28/15 References updated. Description section revised. Policy Statement remains unchanged. (td)

12/30/15 References update. Specialty Matched Consultant Advisory Panel review 11/18/2015. Medical Director review 11/2015. Policy Statement remains unchanged. (td)

4/29/16 Description section revised. Policy Guidelines revised extensively. References updated. (td)

12/30/16 References updated. Specialty Matched Consultant Advisory Panel review 11/2016. Medical Director review 11/2016. (jd)

12/15/17 References updated. Specialty Matched Consultant Advisory Panel 11/2017. Medical Director review 11/2017. (jd)

12/14/18 Minor revisions. References updated. Specialty Matched Consultant Advisory Panel 11/2018. Medical Director review 11/2018. (jd)

12/31/19 References updated. Specialty Matched Consultant Advisory Panel 11/2019. Medical Director review 11/2019. (jd)

12/8/20 References updated. Specialty Matched Consultant Advisory Panel 11/2020. Medical Director review 11/2020. (jd)

11/30/21 Specialty Matched Consultant Advisory Panel 11/2021. Medical Director review 11/2021. (jd)

11/29/22 References updated. Specialty Matched Consultant Advisory Panel 11/2022. Medical Director review 11/2022. (tm)

12/29/23 Description, Policy Guidelines and References updated. Specialty Matched Consultant Advisory Panel 11/2023. Medical Director review 11/2023. (tm)

12/17/24 Policy Guidelines and References updated. Specialty Matched Consultant Advisory Panel 11/2024. Medical Director review 11/2024. (tm)