

MEDICAL POLICY

POLICY TITLE	ADJUNCTIVE TECHNIQUES FOR SCREENING, SURVEILLANCE, AND RISK CLASSIFICATION OF BARRETT ESOPHAGUS AND ESOPHAGEAL DYSPLASIA
POLICY NUMBER	MP 2.390

CLINICAL BENEFIT	☐ MINIMIZE SAFETY RISK OR CONCERN. ☒ MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. ☐ ASSURE APPROPRIATE LEVEL OF CARE. ☐ ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. ☐ ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. ☐ ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
Effective Date:	RETIRED 7/1/2026

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I. POLICY

Wide-area transepithelial sampling with three-dimensional computer-assisted analysis (WATS3D) is considered **investigational** for all indications, including but not limited to the screening and surveillance of Barrett esophagus and esophageal dysplasia.

EsoCheck and Esoguard are considered **investigational** for the screening and surveillance of Barrett esophagus and esophageal dysplasia.

TissueCypher is considered **investigational** for assessing the risk of progression to high-grade dysplasia or esophageal adenocarcinoma in individuals with Barrett esophagus.

BarreGen is considered **investigational** for assessing the risk of progression to high-grade dysplasia or esophageal adenocarcinoma in individuals with Barrett esophagus.

There is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with these procedures.

Cross-References:

MP 1.118 Endoscopic Radiofrequency Ablation or Cryoablation for Barrett's Esophagus

MP 2.266 Molecular Testing for the Management of Pancreatic Cysts and Solid Pancreaticobiliary Lesions

MP 4.019 Oncological Applications of Photodynamic Therapy including Barrett's Esophagus

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II. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below

FEP PPO - Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

<https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies> .

III. DESCRIPTION/BACKGROUND

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Barrett Esophagus

Barrett esophagus (BE) is a condition in which the squamous epithelium that normally lines the esophagus is replaced by specialized columnar-type epithelium known as intestinal metaplasia in response to irritation and injury caused by gastroesophageal reflux disease (GERD). Barrett esophagus occurs in the distal esophagus. It may involve any length of the esophagus, be focal or circumferential, and is visualized on endoscopy with a different color than background squamous mucosa. Confirmation of BE requires a biopsy of the columnar epithelium and microscopic identification of intestinal metaplasia. The prevalence of BE in the United States is estimated at 5.6%. Risk factors associated with the development of BE include GERD, male gender, central obesity, and age over 50 years. The diagnosis of GERD is associated with a 10% to 15% risk of BE. However, a population-based analysis from Sweden observed that 40% of the study cohort with esophageal cancer reported no prior history of GERD symptoms.

Cancer Risk and Management

Intestinal metaplasia is a precursor to esophageal adenocarcinoma, and patients with BE are at a 40-fold increased risk for developing this disease compared to the general population.

However, there are few data to guide recommendations about management and surveillance, and many issues are controversial. Guidelines from the American College of Gastroenterology (ACG), and a consensus statement from an international group of experts (Benign Barrett's and Cancer Taskforce) on the management of BE are published. The ACG recommendations for surveillance are stratified by the presence and grade of dysplasia.

When no dysplasia is detected, ACG has reported the estimated risk of progression to cancer ranges from 0.2% to 0.5% per year and endoscopic surveillance every 3 to 5 years is recommended. For low-grade dysplasia, the estimated risk of progression is 0.7% per year, and endoscopic therapy is preferred; however, endoscopic surveillance every 12 months is considered an acceptable alternative. It is recommended that both options are discussed with the patient. Precise estimates of cancer risk are not available for individuals with low-grade dysplasia due to large disparities among studies on its natural history. Interobserver variability in

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the diagnosis of low-grade dysplasia with standard biopsy may be responsible, with expert pathologists commonly downgrading initial diagnoses made by community pathologists.

The Benign Barrett's and Cancer Taskforce consensus group did not endorse routine surveillance for people without dysplasia and was unable to agree on surveillance intervals for low-grade dysplasia.,

For high-grade dysplasia, the estimated risk of progression is about 7% per year, and ACG has recommended endoscopic eradication therapy, with the type of procedure dependent on patient age and life expectancy, comorbidities, the extent of dysplasia, local expertise in surgery and endoscopy, and patient preference. Approximately 40% of patients with high-grade dysplasia on biopsy are found to have associated carcinoma in the resection specimen.

For patients who are indefinite for dysplasia, a repeat endoscopy should be performed at 3 to 6 months following optimization of acid suppressive medications. A surveillance interval of 12 months is recommended if an indefinite for dysplasia reading is confirmed on repeat endoscopy in these individuals. Many patients who are indefinite for dysplasia show regression to nondysplastic BE with subsequent endoscopic evaluation. It is unclear whether some cases of regression are observed due to sampling error.

IV. RATIONALE

For individuals with a history of Barrett esophagus (BE) who receive standard surveillance with adjunctive WATS3D, the evidence includes a meta-analysis of studies of diagnostic yield, a randomized controlled trial, a physician impact study, a decision analytic model, and a retrospective analysis of the manufacturer database. Relevant outcomes are test validity, overall survival, disease-specific survival, change in disease status, and quality of life. A meta-analysis reported incremental diagnostic yields of 6.9% and 2.4% for any dysplasia or esophageal adenocarcinoma (EAC) or high-grade dysplasia (HGD)/EAC, respectively. These studies are limited by heterogeneity in classification and reporting of test results and selection bias stemming from the enrichment of patients with a prior history of dysplasia. It is also unclear to what extent results obtained from academic centers are generalizable to community-based settings, where adherence to endoscopic biopsy guidelines is poor. In discordant cases where BE or dysplasia were identified only by WATS3D, significant physician management changes included initiation of invasive treatments. Health outcomes stemming from management changes were not reported, and risks associated with overdiagnosis and overtreatment require elucidation. Follow-up data on disease progression in these patients are limited. A retrospective analysis of the manufacturer database found a disease progression rate of 5.79% per patient-year (95% CI, 1.02% to 10.55%) for baseline low-grade dysplasia diagnoses via WATS3D sampling; however, study interpretation is limited as only 16 cases (0.33%) of progression defined as high-grade dysplasia or esophageal adenocarcinoma on follow-up forceps biopsy were identified. A RCT enrolling patients with a recent history of dysplasia reported an absolute increase of 10% in the diagnostic yield of HGD/EAC but did not report on long-term disease progression or mortality outcomes. No direct evidence of clinical utility was identified. Because combined use of WATS3D with standard

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surveillance is intended to replace the current standard of care for guiding patient management decisions regarding initiation of treatment or surveillance, direct evidence of clinical utility is required. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals at increased risk of BE who undergo standard screening with adjunctive WATS3D, the evidence includes a meta-analysis of studies of diagnostic yield, a physician impact study, a decision analytic model, and a retrospective analysis of the manufacturer database. Relevant outcomes are test validity, overall survival, disease-specific survival, change in disease status, and quality of life. A meta-analysis reported incremental diagnostic yields of 7.2% and 2.1% for any dysplasia/EAC or HGD/EAC, respectively. However, available studies have incomplete descriptions of selection criteria, and it is unclear whether study patients are at increased risk as defined by guideline recommendations for screening. In fact, 2 studies were enriched with women in whom screening is generally not recommended by society guidelines. These studies also noted that detected cases of BE in short-segment patients may actually reflect intestinal metaplasia of the cardia, which is thought to carry a significantly lower risk of cancer development compared to traditional BE. In discordant cases where BE or dysplasia were identified only by WATS3D, significant physician management changes included initiation of invasive treatments. Health outcomes from management changes were not reported, and risks associated with overdiagnosis and overtreatment require elucidation. Follow-up data on disease progression in these patients are limited. A retrospective analysis of the manufacturer database found a disease progression rate of 5.79% per patient-year (95% CI, 1.02% to 10.55%) for baseline low-grade dysplasia diagnoses via WATS3D sampling; however, study interpretation is limited as only 16 cases (0.33%) of progression defined as high-grade dysplasia or esophageal adenocarcinoma on follow-up forceps biopsy were identified. No direct evidence of clinical utility was identified. Because combined use of WATS3D with standard screening is intended to replace the current standard of care for guiding patient management decisions regarding initiation of treatment or surveillance, direct evidence of clinical utility is required. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals at increased risk of BE who undergo screening with adjunctive EsoGuard and EsoCheck, the evidence includes observational studies of diagnostic accuracy and clinical utility. Relevant outcomes are test validity, overall survival, disease-specific survival, change in disease status, and quality of life. Studies have reported sensitivities of 85% to 92.9% and specificities of 72.2% to 85% for detecting BE and BE-related neoplasia. Clinical utility studies have shown high concordance (97.9% to 98.8%) between EsoGuard results and endoscopy referral decisions but lack comprehensive follow-up data on confirmatory endoscopy outcomes. In cases where BE or esophageal adenocarcinoma were identified by EsoGuard, management changes included referral for invasive confirmatory procedures, but health outcomes from these changes were not reported. Risks associated with overdiagnosis and overtreatment require elucidation. No direct evidence of clinical utility was identified. Because EsoGuard and EsoCheck are intended to guide patient management decisions regarding referral for confirmatory endoscopy and potentially replace or supplement current screening standards, direct evidence of improvement in health

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outcomes is required. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with non-dysplastic, indefinite dysplasia, or low-grade dysplasia BE who undergo standard screening with adjunctive TissueCypher, the evidence includes multiple clinical validity studies and physician impact studies. Relevant outcomes are test validity, overall survival, disease-specific survival, change in disease status, and quality of life. Clinical validity studies have reported sensitivities ranging from 29% to 71% and specificities between 79% to 95% for predicting progression to high-grade dysplasia or esophageal adenocarcinoma. Hazard ratios for high-risk versus low-risk groups ranged from 3.23 to 5.26, indicating increased progression risk for individuals classified as high-risk by TissueCypher. The assay showed improved risk stratification compared to expert pathologist reviews in several studies. Clinical utility studies have focused on the impact of TissueCypher results on patient management decisions. One author found that TissueCypher results influenced more than half of management decisions, leading to both upstaging and downstaging of treatment approaches. Another study reported that incorporating TissueCypher results significantly increased the percentage of patients receiving guideline-appropriate management compared to pathology review alone. A randomized trial using simulated patients found that physicians with access to TissueCypher results were more likely to correctly assess progression risk and offer guideline-concordant treatment. However, these studies primarily relied on simulated cases or management decision changes, and long-term patient outcomes resulting from TissueCypher-guided management have not been directly assessed. The use of adjunct TissueCypher is intended to classify individuals with BE based on their risk of progression to high-grade dysplasia or esophageal adenocarcinoma, this can change patient management decisions regarding the initiation of treatment such as esophageal eradication therapy or enhanced surveillance. Therefore, direct evidence of improvement in health outcomes is required. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have Barrett esophagus who receive standard prognostic techniques plus topographic genotyping (BarreGEN molecular testing), no studies were identified. the evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

V. DISCLAIMER

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Capital Blue Cross' medical policies are used to determine coverage for specific medical technologies, procedures, equipment, and services. These medical policies do not constitute medical advice and are subject to change as required by law or applicable clinical evidence from independent treatment guidelines. Treating providers are solely responsible for medical advice and treatment of members. These policies are not a guarantee of coverage or payment. Payment of claims is subject to a determination regarding the member's benefit program and eligibility on the date of service, and a determination that the services are medically necessary and appropriate. Final processing of a claim is based upon the terms of

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contract that applies to the members' benefit program, including benefit limitations and exclusions. If a provider or a member has a question concerning this medical policy, please contact Capital Blue Cross' Provider Services or Member Services.

VI. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement. The codes need to be in numerical order.

Considered investigational for WATS3D, EsoCheck, EsoGuard, TissueCypher, or BarreGen; therefore, not covered:

Procedure Codes							
88104	88305	88312	88361	0108U	0114U		

ICD-10-CM Diagnosis Code	Description
K22.70	Barrett's esophagus without dysplasia
K22.710	Barrett's esophagus with low grade dysplasia
K22.711	Barrett's esophagus with high grade dysplasia
K22.719	Barrett's esophagus with dysplasia, unspecified
K22.89	Other specified disease of esophagus
K22.9	Disease of esophagus, unspecified

VII. REFERENCES

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MP 2.390	07/17/2024 Major Review. New Policy
	01/23/2025 Minor Review. Policy title changed to "Adjunctive Techniques for Screening, Surveillance, and Risk Classification of Barrett Esophagus and Esophageal Dysplasia." Three new policy statements were added: EsoCheck and Esoguard are considered investigational for the screening and surveillance of Barrett esophagus and esophageal dysplasia. TissueCypher is considered investigational for assessing the risk of progression to high-grade dysplasia or esophageal adenocarcinoma in individuals with Barrett esophagus. BarreGen is considered investigational for the risk stratification of Barrett esophagus and esophageal dysplasia. Background, rationale, references updated. Added codes 0108U and 0114U as INV.
	07/18/2025 Administrative Update. Removed Benefit Variations Section and updated Disclaimer.
	03/05/2026 Retirement Review. EviCore Delegation.

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