Medical Coverage Policy

Effective Date.....10/15/2024
Next Review Date.....10/15/2025
Coverage Policy Number..... 0577

Mucosal Integrity Testing

Table of Contents

Related Coverage Resources

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy

will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses esophageal mucosal integrity testing via transoral electrical impedance which includes esophagoscopy or esophagogastroduodenoscopy (HCPCS code C9777) (MiVu™ Mucosal Integrity Testing System).

Coverage Policy

Esophageal mucosal integrity testing by electrical impedance is considered experimental, investigational, or unproven.

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

General Background

Esophageal mucosal integrity testing has been proposed as a method to diagnosis gastroesophageal reflux disease (GERD) and eosinophilic esophagitis (EoE). Mucosal Integrity is affected by the presence of dilated intercellular spaces (DIS), or spongiosis, which affects paracellular permeability of the esophageal lumen. DIS is an important histologic feature in GERD and EoE where the degree of dilation inversely correlates with MI measurements (i.e., lower impedance values occur with increasing DIS). The diagnosis of GERD may be based on clinical symptoms alone in patients with heartburn and/or regurgitation. However, patients may require additional evaluation if they have alarm features, risk factors for Barrett's esophagus, or abnormal gastrointestinal imaging performed for evaluation of their symptoms. An upper endoscopy is indicated in patients with suspected GERD to evaluate alarm features or abnormal imaging. An upper endoscopy may also be performed to screen for Barrett's esophagus in patients with risk factors. On upper endoscopy, biopsies can be performed and should target any areas of suspected metaplasia, dysplasia, or, in the absence of visual abnormalities, normal mucosa to evaluate for eosinophilic esophagitis.

According to the vendor's website, the MiVu™ Mucosal Integrity Testing System (Diversatek Healthcare, Inc.) utilizes a balloon probe and proprietary software to instantly detect changes in esophageal mucosal integrity during endoscopy. The MiVu™ Balloon Probe incorporates both radial and axial sensors mounted at 180-degree intervals along a 10 cm segment of the esophagus to measure esophageal mucosal integrity. Real time impedance values, a mucosal integrity contour

pattern and disease probability are displayed which distinguishes various esophageal pathologies (GERD, EoE, or Non-GERD).

U.S. Food and Drug Administration (FDA)
On December 23, 2019, the Mucosal Integrity Conductivity (MI) Test System (Diversatek Healthcare Inc.) received FDA De Novo approval as a Class II device as an esophageal tissue characterization system. An esophageal tissue characterization system is a device intended for obtaining measurements of electrical properties within esophageal tissue.

MiVu™ Esophageal Endo Cap Esophageal tissue characterization system (Diversatek Healthcare) received 510(k) approval on April 25, 2023 (K230056). The Diversatek Healthcare MiVu Esophageal Endo Cap is the candidate accessory device for use with the approved predicate Diversatek Healthcare's MiVu Mucosal Integrity Testing system (MiVu System). The MiVu Esophageal Endo Cap is a new patient-contacting accessory that will be used in place of the MiVu Balloon Probe already approved as part of the MiVu System.

The Indications for Use state, "The MiVu Mucosal Integrity Testing System is indicated for use by gastroenterologists, surgeons, and medical personnel trained in endoscopic procedures during an endoscopy to obtain real-time measurement of esophageal epithelial integrity as an adjunct for the evaluation of esophageal disorders. The device is not for use as a sole diagnostic screening tool."

Literature Review

Patel et al. (2019) reported on a prospective study to evaluate the ability of a balloon-incorporated mucosal impedance (MI) catheter to detect and evaluate esophageal disorders, including gastroesophageal reflux disease (GERD) and eosinophilic esophagitis (EoE).the study included 69 patients undergoing esophagogastroduodenoscopy with or without wireless pH monitoring. Patients were classified as having GERD (erosive esophagitis or abnormal pH; n = 24), EoE (confirmed with pathology analysis of tissues from both distal and proximal esophagus; n = 21), or non-GERD (normal results from esophagogastroduodenoscopy and pH tests; n = 24). Receiver operating characteristic curves (ROC) and area under the ROC curve (AUC) were used to compare the accuracy of balloon MI in diagnosis. Probabilities of assignment to each group (GERD, non-GERD, or EoE) were estimated using multinomial logistic regression. Association between MI patterns and diagnoses were validated using data from patients seen at 3 separate institutions. The MI pattern along the esophageal axis differed significantly ($p<0.01$) among patients with GERD, EoE and non-GERD. Patients with non-GERD had higher MI values along all measured segments. The MI pattern for GERD was easily distinguished from that of EoE: in patients with GERD, MI values were low in the distal esophagus and normalized along the proximal esophagus, whereas in patients with EoE, measurements were low in all segments of the esophagus. Intercept and rate of rise of MI value (slope) as distance increased from the squamo-columnar junction identified patients with GERD with an AUC = 0.69, patients with EoE with an AUC of 0.89, and patients with non-GERD with an AUC = 0.84 in the development cohort. One patient had an adverse event of mild chest pain after the procedure and was discharged from the hospital without further events.

Choksi et al. (2018) reported on a retrospective analysis of 91 patients to quantify mucosal impedance (MI) along the esophagus and identify patterns that differentiated patients with and without gastroesophageal reflux disease (GERD) from those with eosinophilic esophagitis (EoE). They set out to determine whether MI values and patterns are sufficient to identify patients with EoE using histologic findings as a reference. During the first endoscopy, MI measurements were obtained at two, five, and 10 cm from the squamocolumnar junction. GERD was confirmed by ambulatory pH tests, and histologic analyses of biopsies were used to confirm EoE. Statistical

modeling was used to identify MI patterns along the esophagus that associated with GERD vs EoE. Findings were validated in a prospective cohort of 49 patients undergoing elective upper endoscopy for dysphagia. It was noted that patients with EoE have a unique MI pattern, with low values along the esophageal axis. MI measurements at five cm could discern patients with normal vs abnormal mucosa with 83% sensitivity and 79% specificity, and patients with EoE vs GERD with 84% sensitivity and 70% specificity; the measurements differentiated the patient populations with the highest level of accuracy of any of the six measurements tested. In the validation study, a rater using the esophageal MI pattern identified patients with EoE with 100% sensitivity and 96% specificity. The study is limited by retrospective nature and lack of randomization.

Lowry et al. (2018) conducted a prospective study to investigate whether mucosal impedance measurements can be used to monitor disease activity in 173 pediatric patients with Eosinophilic esophagitis (EoE). Mucosal impedance was measured at three locations in the esophagus in pediatric patients (1-18 years old; 32 with active EoE, 10 with inactive EoE, 32 with nonerosive reflux disease [NERD]) and 53 children with symptoms but normal findings from histologic analyses (controls) undergoing routine esophagogastroduodenoscopy. Pathologists reviewed biopsies per routine protocol, determined eosinophilic density, and graded spongiosis on an ordinal visual scale. Mucosal impedance measurements were compared within patient groups. The primary outcome was correlation of mucosal impedance measurements with disease activity, based on severity of spongiosis and eosinophil counts. Mucosal impedance measurements were significantly lower in patients with active EoE at 2, 5, and 10 cm above the squamo-columnar junction (median values of 1069, 1368, and 1707, respectively) compared to patients with inactive EoE (median values of 3663, 3657, and 4494, respectively), NERD (median values of 2754, 3243, and 4387), and controls (median values of 3091, 3760, and 4509) ($P < 0.001$ for all comparisons to patients with active EoE). Inverse correlations were found between mucosal impedance measurements and eosinophil count ($P < 0.001$), and spongiosis severity ($P < 0.001$). The authors concluded that mucosal impedance measurements may provide immediate information about mucosal inflammation in children and this needs to be confirmed by further, prospective studies.

An UpToDate review on "Clinical manifestations and diagnosis of gastroesophageal reflux in adults" (Kahrilas, 2023) does not mention mucosal integrity testing or MiVu catheter placement as a management tool.

Professional Societies/Organizations
American College of Gastroenterology (ACG): The ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease states "Mucosal integrity testing, e.g., is available commercially but is not developed sufficiently to warrant discussion in this guideline" (Katz, et al., 2022).

The American Gastroenterological Association (AGA): The AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: Expert Review (Yadlapati, et al., 2022) does not address mucosal integrity testing.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	No determination found.	
LCD		No determination found.	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare & Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Experimental/Investigational/Unproven:

HCPCS Codes	Description
C9777	Esophageal mucosal integrity testing by electrical impedance, transoral includes esophagoscopy or esophagogastroduodenoscopy

***Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.**

References

1. Choksi Y, Lal P, Slaughter JC, Sharda R, Parnell J, Higginbotham T, Vaezi MF. Esophageal Mucosal Impedance Patterns Discriminate Patients With Eosinophilic Esophagitis From Patients With GERD. Clin Gastroenterol Hepatol. 2018 May;16(5):664-671.e1.
2. Clarke JO, Ahuja NK, Chan WW, Gyawali CP, Horsley-Silva JL, Kamal AN, et al. Mucosal impedance for esophageal disease: evaluating the evidence. Ann N Y Acad Sci. 2020 Dec;1481(1):247-257.
3. Diversatek Healthcare. MiVu™ Mucosal Integrity Testing System. (product information). Accessed July 2024. Available at URL address: https://diversatekhealthcare.com/mucosal-integrity-mivu-2/
4. Kahrilas PJ. Clinical manifestations and diagnosis of gastroesophageal reflux in adults. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed Jul 2022; literature current through Jul 2024.
5. Katz PO, Dunbar KB, Schnoll-Sussman FH, Greer KB, Yadlapati R, Spechler SJ. ACG Clinical Guideline for the Diagnosis and Management of Gastroesophageal Reflux Disease. Am J Gastroenterol. 2022 Jan 1;117(1):27-56.
6. Lei WY, Vaezi MF, Naik RD, Chen CL. Mucosal impedance testing: A new diagnostic testing in gastroesophageal reflux disease. J Formos Med Assoc. 2020 Nov;119(11):1575-1580.
7. Lowry MA, Vaezi MF, Correa H, Higginbotham T, Slaughter JC, Acra S. Mucosal Impedance Measurements Differentiate Pediatric Patients With Active Versus Inactive Eosinophilic Esophagitis. J Pediatr Gastroenterol Nutr. 2018 Aug;67(2):198-203.
8. Matsumura T, Arai M, Ishigami H, Fujie M, Ishikawa K, Akizue N, et al. Evaluation of Esophageal Mucosal Integrity in Patients with Gastroesophageal Reflux Disease. Digestion. 2018;97(1):31-37.
9. Patel DA, Higginbotham T, Slaughter JC, Aslam M, Yuksel E, Katzka D. Development and Validation of a Mucosal Impedance Contour Analysis System to Distinguish Esophageal Disorders. Gastroenterology. 2019 May;156(6):1617-1626.e1.
10. U.S. Food and Drug Administration (FDA). Mucosal Integrity Conductivity (MI) Test System. DEN180067, De novo classification. Accessed July 2024. Available at URL address: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/denovo.cfm?id=DEN180067

11. U.S. Food and Drug Administration (FDA). MiVu™ Esophageal Endo Cap Esophageal tissue characterization system. 510(k) approval April 25, 2023 (K230056). Accessed July 2024. Available at URL address: https://www.accessdata.fda.gov/cdrh_docs/pdf23/K230056.pdf
12. Vanuytsel T, Tack J, Farre R. The Role of Intestinal Permeability in Gastrointestinal Disorders and Current Methods of Evaluation. Front Nutr. 2021 Aug 26;8:717925.
13. Xie C, Sifrim D, Li Y, Chen M, Xiao Y. Esophageal Baseline Impedance Reflects Mucosal Integrity and Predicts Symptomatic Outcome With Proton Pump Inhibitor Treatment. J Neurogastroenterol Motil. 2018 Jan 30;24(1):43-50.
14. Yang YX, Brill J, Krishnan P, Leontiadis G; American Gastroenterological Association Clinical Practice Guidelines Committee. American Gastroenterological Association Institute Guideline on the Role of Upper Gastrointestinal Biopsy to Evaluate Dyspepsia in the Adult Patient in the Absence of Visible Mucosal Lesions. Gastroenterology. 2015 Oct;149(4):1082-7.
15. Yadlapati R, Gyawali CP, Pandolfino JE; CGIT GERD Consensus Conference Participants. AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: Expert Review. Clin Gastroenterol Hepatol. 2022 May;20(5):984-994.e1. Erratum in: Clin Gastroenterol Hepatol. 2022 Sep;20(9):2156.

Revision Details

Type of Revision	Summary of Changes	Date
Annual review	• No clinical policy statement changes.	10/15/2024