Priority Health

MEDICAL POLICY
No. 91483-R13

GASTROESOPHAGEAL REFLUX DISEASE (GERD) AND BARRETT'S ESOPHAGUS

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Date Of Origin: February 25, 2004	**Status: Current**

I. POLICY/CRITERIA

Treatment for gastroesophageal reflux disease (GERD)

A. Transoral incisionless fundoplication (TIF) for gastroesophageal reflux disease (GERD) for individuals with normal esophageal motility (by either manometry or video esophagogram) is medically necessary for any of the following indications:

1. Anatomic disruption of the gastroesophageal (GE) flap valve to a Hill Grade II-III.
2. Persistent GERD symptoms despite proton pump inhibitors (PPI) therapy.
3. Evidence of one of the following while on PPI therapy:
   a. Erosive esophagitis (erosions or ulcerations during endoscopy)
   b. Abnormal ambulatory pH study
   c. Biopsy confirmed changes characteristic of reflux esophagitis
4. Contraindications for TIF include:
   a. Active esophago-gastro-duodenal ulcer disease
   b. BMI $\geq$ 35
   c. Hiatal hernia > 2 cm
   d. Esophagitis grade D or Barrett's esophagitis
   e. Esophageal ulcer
   f. Fixed esophageal stricture or narrowing
   g. Gastric outlet obstruction or stenosis
   h. Gastroparesis or delayed gastric emptying confirmed by solid-phase gastric emptying study if patient complains of postprandial satiety during assessment.
   i. History of previous resective gastric or esophageal surgery, cervical spine fusion, Zenker's diverticulum, esophageal epiphrenic diverticulum, achalasia, scleroderma or dermatomyositis, eosinophilic esophagitis, > 2 dilations for esophageal stricture, or cirrhosis.
   j. Portal hypertension and/or varices

B. **The Stretta** radiofrequency energy procedure for the treatment of GERD may be considered medically necessary for patients 18 years or older when all of the following clinical criteria are met (1 or 2 and 3 below):

1. Member must have all of the following:
   a. Daily gastroesophageal reflux disease (GERD) > 6 months as evidenced by **one** of the following:
      i. pH study (performed off medication) showing pathologic acid exposure (pH <4 more than 4% of a 24- hour period OR DeMeester score >14.7), ***OR***
      ii. upper GI endoscopy showing Grade A or B esophagitis (Los Angeles classification), ***OR***
      iii. abnormal reflux as determined by impedance testing, ***OR***
      iv. biopsy confirmed reflux esophagitis
   b. Esophageal manometry demonstrating **both** of the following:
      i. normal peristalsis (e.g. lack of frequent large breaks in peristaltic propagation, or bolus clearance > 70%, or contractility > 500), ***AND***
      ii. normal sphincter relaxation (i.e. residual pressure $\leq$8 mmHg)
   c. Symptoms of heartburn refractory to daily appropriate dose anti-secretory therapy.

   OR

2. Member has been diagnosed with:
   a. reflux related aspiration pneumonia, OR
   b. laryngopharyngeal reflux

   AND

3. Member does not have any of following:
   a. American Society of Anesthesiologists (ASA) IV classification
   b. Barrett's esophagus,
   c. Esophagitis grade C or D (Los Angeles classification)
   d. Hiatal hernia >2cm
   e. Autoimmune disease
   f. Collagen vascular disorder
   g. Coagulation disorder
   h. Current anticoagulant therapy
   i. Life threatening disorder with life expectancy <1 year
   j. Achalasia
   k. Current pregnancy

Credentialing:

1. Physician must be privileged in Esophagogastroduodenoscopy (EGD) and have completed the manufacturer's training program for Stretta.

2. Documentation of training must be available upon request.

C. **Magnetic sphincter augmentation (MSA) with the LINX** device may be medically necessary for the treatment of GERD when all of the following are met:

1. 18 - 74 years of age
2. Body Mass Index (BMI) ≤35
3. Documented typical symptoms of GERD for longer than 6 months (regurgitation or heartburn which is defined as a burning epigastric or substernal pain which responds to acid neutralization or suppression)
4. Member is refractory to ideal medical management (requires twice daily proton pump inhibitor or other anti-reflux drug therapy, diet and lifestyle change discussed).
5. Hiatal hernia ≤3 cm as determined by endoscopy
6. Total Distal Ambulatory Esophageal pH< 4 for ≥ 4.5% of the time with discontinuation of any GERD medications for at least 7 days prior to testing.
7. Distal esophageal motility within normal range, as defined by either:
   a. Conventional manometry (average of sensors 3 and 4 is ≥ 35 mmHg peristaltic amplitude on wet swallows or ≥70% (propulsive) peristaltic sequences; OR,
   b. High resolution manometry (HRM):
      i. Distal contractile integral 500 – 5000 mm Hg cm s; AND,
      ii. Distal latency > 4.5 s
8. Symptomatic improvement on PPI therapy demonstrated by
a. GERD-Health-Related Quality of Life (GERD-HRQL) score of ≤ 10 on proton-pump inhibitors and ≥ 15 off PPIs, or
b. ≥ 6 point improvement when comparing their on PPI and off PPI GERD-HRQL score
9. None of the following:
   a. Current electrical implant or metallic abdominal implant
   b. Diagnosed with Scleroderma
   c. Diagnosed with an esophageal motility disorder such as but not limited to Achalasia, Nutcracker Esophagus, or Diffuse Esophageal Spasm or Hypertensive LES
   d. Diagnosed psychiatric disorder (e.g., bipolar, schizophrenia, etc.), not including depression on appropriate medication(s), would require statement of clearance from the treating Behavioral Health team.
   e. Esophageal or gastric varices
   f. Esophagitis - Grade C or D (Los Angeles Classification)
   g. History of or known Barrett's Esophagus

h. History of gastroesophageal surgery, anti-reflux procedures, including endoscopic anti-reflux procedures
i. History of or known esophageal stricture or gross esophageal anatomic abnormalities (Schatzki's ring, obstructive lesions, etc.)
j. Suspected or confirmed esophageal or gastric cancer
k. Symptoms of dysphagia more than once per week within the last 3 months.
l. Life expectancy less than 3 years
m. Pregnant or breastfeeding
n. Suspected or known allergies to titanium, stainless steel, nickel or ferrous materials

10. Prior authorization by Priority Health.

Credentialing:

1. Physician must be privileged in foregut procedures and have completed the manufacturer's device specific training and device specific proctoring from designated LINX Preceptor (Torax Medical).
2. Documentation of training must be available upon request.

D. Priority Health considers other treatments for GERD as investigational and experimental, or not medically necessary. These include, but are not limited to the following:
1. Endoscopic suturing or implantation of inert polymers for the treatment of gastroesophageal reflux are considered experimental and investigational:
   a. Bard EndoCinch Suturing System (C.R. Bard Inc.) Angelchik anti-reflux prosthesis
   b. Enteryx
   c. Endoscopic Plicator System (NDO Surgical, Inc.) and the Syntheon ARD Plicator (Syntheon)
   d. Durasphere (Carbon Medical Technologies), the Gatekeeper Reflux Repair System (Medtronic, Inc.), an endoscopically-implanted injectable esophageal prosthesis, and the Plexiglas polymethylmethacrylate (PMMA) microspheres (Arkema Inc.)

The evidence does not permit conclusions on health outcomes or if endoscopic suturing or implantation of inert polymers are as beneficial as established alternatives. Case series data are inadequate to demonstrate improvement in health outcome. The procedures have not been compared to Nissen fundoplication in controlled trials, and the risks and benefits of the procedures compared to Nissen fundoplication are not established. There is no long-term outcome data to show the durability of these procedures.

E. The following device is considered experimental and investigational for the treatment of GERD or any other condition:

1. Reza Band Upper Esophageal Sphincter Assist Device

Treatment for Barrett's Esophagus (BE)

F. **Endoscopic Mucosal Resection and/or Thermal Ablation Treatment (i.e., Barrx)** or **Photodynamic Therapy** for Barrett's Esophagus (BE) is medically necessary when the following is present:

1. Dysplastic Barrett's Esophagus and/or early esophageal adenocarcinoma (EAC).
2. The data available at present is insufficient to support these modalities in non-dysplastic Barrett's esophagus.

G. Any of the following ablative or surgical interventions are considered experimental and investigational for the treatment of members with Barrett's Esophagus:

1. Argon plasma coagulation
2. Chemoradiation therapy
3. Cryotherapy
4. Laser therapy
5. Multi-polar electro-coagulation
6. Ultrasonic therapy

H. Any of the following tests are considered experimental and investigational for the diagnosis or management of Barrett's Esophagus:

1. Capsule endoscopy of the esophagus
2. Confocal laser endomicroscopy and Fuji Intelligent Chromo Endoscopy (FICE)
3. Genetic mutation analysis
4. Methylation biomarkers and microRNA tests.
5. Wide-area transepithelial sampling (WATS3D)
6. TissueCypher

II. MEDICAL NECESSITY REVIEW

Prior authorization for certain drug, services, and procedures may or may not be required. In cases where prior authorization is required, providers will submit a request demonstrating that a drug, service, or procedure is medically necessary. For more information, please refer to the Priority Health Provider Manual.

III. APPLICATION TO PRODUCTS

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

- **HMO/EPO:** ***This policy applies to insured HMO/EPO plans.***
- **POS:** ***This policy applies to insured POS plans.***
- **PPO:** ***This policy applies to insured PPO plans. Consult individual plan documents as state mandated benefits may apply. If there is a conflict between this policy and a plan document, the provisions of the plan document will govern.***
- **ASO:** ***For self-funded plans, consult individual plan documents. If there is a conflict between this policy and a self-funded plan document, the provisions of the plan document will govern.***
- **INDIVIDUAL:** ***For individual policies, consult the individual insurance policy. If there is a conflict between this medical policy and the individual insurance policy document, the provisions of the individual insurance policy will govern.***
- **MEDICARE:** ***Coverage is determined by the Centers for Medicare and Medicaid Services (CMS) and/or the Evidence of Coverage (EOC); if a coverage determination has not been adopted by CMS, this policy applies.***
- **MEDICAID/HEALTHY MICHIGAN PLAN:** ***For Medicaid/Healthy Michigan Plan members, this policy will apply. Coverage is based on medical necessity criteria being met and the appropriate code(s) from the coding section of this policy being included on the Michigan Medicaid Fee Schedule located at: http://www.michigan.gov/mdch/0,1607,7-132-2945_42542_42543_42546_42551-159815--,00.html. If there is a discrepancy between this policy and the Michigan Medicaid Provider Manual located at: http://www.michigan.gov/mdch/0,1607,7-132-2945_5100-87572--,00.html, the Michigan Medicaid Provider Manual will govern. For Medical Supplies/DME/Prosthetics and Orthotics, please refer to the Michigan Medicaid Fee Schedule to verify coverage.***

IV. DESCRIPTION/ BACKGROUND

Gastroesophageal reflux disease (GERD), also known as reflux esophagitis, is probably the most prevalent clinical condition that arises from the gastrointestinal (GI) tract. There are two principal factors involved in esophageal reflux: (i) the GI contents and (ii) the anti-reflux mechanism, which is comprised of the lower esophageal sphincter (LES) and the anatomic configuration of the gastroesophageal junction. Reflux occurs when the gradient between the LES pressure and the intragastric pressure is compromised as a result of a transient or sustained reduction in the former, or an elevation in the latter. Most patients with GERD have decreased LES pressures. However, some patients have normal LES pressures, but their sphincters relax inappropriately, thus resulting in refluxes.

The initial treatment of GERD is geared toward reducing esophageal refluxes. Antacids, H2-receptor antagonists, as well as dietary and lifestyle modifications have been used for such purposes. For patients who fail initial treatment, proton pump inhibitors (e.g., lansoprazole and omeprazole) should be tried. When these standard medical therapies fail, surgery may be considered.

Traditional procedures were designed to raise the pressure within the LES by wrapping a portion or all of the cardia stomach around the esophagus. With the advent of

laparoscopic anti-reflux surgery, the two most common procedures are the Nissen fundoplication and the Toupet partial fundoplication. Anti-reflux surgery has been reported to have an efficacy rate of 90%. These operations are usually performed on the same day of hospital admission and take approximately 90 minutes. In general, patients are discharged from the hospital on the second postoperative day and can return to work in 7 to 10 days. Anti-reflux surgery can be associated with complications. The most common complications are dysphagia and an inability to belch or vomit, occurring in 4 to 11% of patients. The ideal candidates for anti-reflux surgery should be young, have typical GERD symptoms (heartburn and regurgitation) with or without a hiatal hernia, have an abnormal ambulatory pH test, have normal esophageal motility studies, and have responded, at least partially, to PPI therapy.

Limitations to the use of fundoplication include the need for surgical expertise, the need for hospitalization and several weeks of postoperative recovery, and the risk of complications and development of new symptoms not present before the surgery. Additionally, many patients treated surgically will need to resume pharmacologic therapy over time as often the surgery does not cure their disease or permanently modify their need for medication use. It is because of the invasiveness, costs, and inherent risks of surgery that an interest in alternative, endoscopic therapies for GERD, has emerged.

Endoscopic, or endoluminal, therapies for GERD are designed to alter structures at the gastroesophageal junction to prevent reflux of gastric contents. Current endoscopic therapies may be classified into three basic categories: (1) radiofrequency energy or radiofrequency thermal ablation; (2) endoscopic or plication suturing; and (3) polymer injection and implantation techniques.

Radiofrequency Energy or Radiofrequency Thermal Ablation: Thermal energy is delivered to the lower esophageal sphincter (LES) using endoscopically placed needles. Proposed mechanism of action is unknown, although it is likely that there is a resultant scarring or neurolysis in the lower esophageal sphincter. The Stretta® System is an example of radiofrequent (RF) thermal energy delivered to the LES using endoscopically placed needles. RF thermal injury purportedly results in ablation of nerve pathways responsible for tLESRs and/or tissue tightening or remodeling of the gastroesophageal junction due to heat-induced collagen contraction. Thus, RF energy may improve LES compliance and inhibit tLESRs. The Stretta procedure was reviewed by the Priority Health Technology Assessment Committee in September 2015. This policy reflects the recommendation of the committee.

Plication/Suturing Techniques: This procedure is also referred to as Endoluminal Gastric Plication (ELGP). A needle puncture device attached to the endoscope creates pleats through a series of sutures passed by a needle through adjoining proximal fundic folds at the gastroesophageal junction. The proposed action is providing a physical barrier to gastric reflux, possibly by increasing the length of the lower esophageal sphincter (LES), decreasing the esophageal luminal diameter, or decreasing the frequency of transient relaxations of the LES (tLESRs). Examples of suture plication (gastroplasty) devices are EndoCinch™ (Bard™ Endoscopic Technologies, Billerica, MA) and the

Endoscopic Suturing Device® (ESD; Wilson-Cook Medical, Winston-Salem, and NC), also called Sew-Right. These devices sometimes are referred to as miniature or endoscopic "sewing machines." With this technology, which uses a transoral flexible endoscopic suturing device to create pleats in the gastroesophageal junction, a needle puncture device attached to the endoscope creates pleats through a series of sutures passed by a needle through adjoining proximal fundic folds, thus, providing a barrier to gastric reflux. A third suture plication device, the full-thickness Endoscopic Plication™ System (EPS; NDO Surgical, Inc., Mansfield, MA) has been designed to inhibit gastroesophageal reflux by placing a transmural plication near the gastroesophageal junction under direct endoscopic visualization to enhance the competency of the gastric cardia. The EPS is an enlarged flexible tube that forms a fundic fold fixation with a single pretied suture implant delivered by the instrument, while retroflexed within the stomach and visually monitored through an inserted endoscope. Thus, plication devices may act by restoring the flap mechanism.

The EndoGastric Solutions (EGS) EsophyX™ System with Serofuse™ Fastener is indicated for use in endoluminal, transoral tissue approximation, full thickness plication and ligation in the GI tract and is indicated for the treatment of symptomatic chronic gastroesophageal reflux disease in patients who require and respond to pharmacological therapy. It is also indicated to narrow the gastroesophageal junction and reduce hiatal hernia ≤ 2cm in size in patients with symptomatic chronic gastroesophageal reflux disease. During TIF 2.0, the EsophyX device is introduced through the mouth and down the throat to the gastroesophageal valve. The device is used to retract the tissue around the base of the esophagus and create a 3-centimeter–long 270° valve with 12 to 23 implantable fasteners. Early versions of this procedure were known as endoluminal fundoplication and TIF 1.0. The current procedure is believed to be most like laparoscopic Nissen fundoplication, which is the current standard care (Ihde, 2020). Laparoscopic fundoplication is effective for the treatment of GERD and is less invasive than open fundoplication, but it still leaves a scar and carries the possibility of complications, such as GERD recurrence, need for repeat surgery, chronic dysphagia, gas, bloating, and inability to belch or vomit (Frazzoni et al., 2014). TIF 2.0 has been available since 2009 and is one of several minimally invasive treatments for GERD that is not fully responsive to medication.

Polymer Injection/Implantation Techniques: These are referred to as bulking techniques as their proposed mechanism of action is to provide bulking support to the sphincter keeping stomach fluids and acids from backing up into the esophagus. It does not affect the stomach's ability to produce acid or other digestive fluids. The procedure is not reversible. There are several polymer injection techniques under investigation, including Enteryx™ injection therapy (Boston Scientific Corp., Natick, MA), in which inert polymer material is injected deep into the submucosal zone beneath the LES to form a ring like "bulking" zone to augment sphincter pressure and decrease tLESRs; the Gatekeeper™ Reflux Repair System (Medtronic, Inc., Minneapolis, MN), which allows endoscopic introduction of an expandable hydrogen prosthesis into the submucosa of the LES zone; and the Plexiglas (polymethylmethacrylate [PMMA]) implantation procedure (Röhm GmbH & Co. KG, Darmstadt, Germany), in which PMMA microspheres are

injected endoscopically by needle under high pressure into the submucosa of the proximal LES zone to provide "bulking" support to the sphincter. At this time, neither Gatekeeper nor PMMA are FDA approved.

On October 14, 2005 the FDA issued a preliminary public health notification recall of all Enteryx™ Procedure Kits and Single Pack Enteryx™ Injectors to health care practitioners stating serious adverse events, including death, occurred in patients treated with Enteryx™ for GERD (FDA, 2005).

Endoscopically based therapies for Barrett's esophagus (BE) are designed to destroy the damaged tissue in the esophagus associated with BE and thus reduce the risk of esophageal cancer in these individuals. There are currently two endoscopically based therapies for BE: (1) Photodynamic Therapy (PDT); (2) Thermal Ablation.

1. **Photodynamic Therapy (PDT):** PDT using porfimer sodium (Photofrin) is an FDA approved treatment for Barrett's esophagus with high grade dysplasia. Porfimer sodium is a light-sensitizing drug (a photosynthesizer) which is administered intravenously or by mouth. The drug concentrates in the Barrett's tissues. The esophageal tissue is then exposed to modified laser light. Photoactivation of the drug then destroys the cells in which is it has been absorbed.

2. **Thermal Ablation (TA):** The goal of this therapy is to ablate dysplastic tissue, reversing the histopathological changes characteristic of BE, and initiating squamous re-epithelialization of the esophagus. Using a controller to limit the amount of heat energy generated, a high-frequency electric current is passed through a heater element for less than a second to destroy the innermost layer of esophageal tissue. The HALO^{360} Coagulation System, which is also referred to as the BÂRRX device, is an example of this technology.

Reza Band Upper Esophageal Sphincter Assist Device: The Reza Band is a non-medication, non-surgical medical device that is externally worn and applies a slight, external pressure to the cricoid cartilage to generate added intraluminal UES pressure to stop reflux from rising above the UES. There is no evidence in the peer-reviewed medical literature to support its effectiveness.

WATS3D

WATS3D biopsy (CDx Diagnostics Inc.) is performed during esophageal endoscopy using a stiff brush that is spun and moved up and down and across abnormal tissue to collect small strips and clumps of cells. Biopsy specimens are stained and analyzed at CDx Diagnostics in a process that includes computerized image analysis of all visible cells, which are displayed with highlighting of suspicious features. The WATS3D biopsy procedure, also referred to as WATS3D, is performed by a gastroenterologist in an outpatient setting during endoscopic examination of the esophagus and is intended as an adjunct to standard 4-quadrant focal biopsies for screening, diagnosis, or surveillance of

patients with known or suspected esophageal precancer (e.g., Barrett's esophagus) or cancer (Hayes, 2023).

The evidence for the use of WATS3D is limited to its utility in diagnostic yield, and it is unclear whether it results in improved patient outcomes. In a prospective, multicenter, randomized controlled trial; 160 patients with BE underwent either forceps biopsy sampling followed by WATS3D or WATS3D followed by biopsy sampling. The primary outcome was rate of detection of high-grade dysplasia/esophageal adenocarcinoma using WATS3D in conjunction with biopsy sampling compared with biopsy sampling alone. Results showed that the addition of WATS to biopsy sampling was feasible and yielded an additional 23 cases of HGD/esophageal adenocarcinoma (absolute increase, 14.4%) (Vennalaganti et al, 2018). In another multicenter prospective trial 4,203 patients underwent WATS3D adjunctively to targeted forceps biopsy and random four-quadrant forceps biopsy. In total, 594 patients were diagnosed with Barrett's esophagus (BE) by forceps biopsy alone, and 493 additional cases were detected by adding WATS, increasing the overall detection of BE by 83%. Low-grade dysplasia (LGD) was diagnosed in 26 patients by forceps biopsy alone, and 23 additional cases were detected by adding WATS3D, increasing the detection of LGD by 88.5% (Gross et al, 2017). Smith et al. (2017) also investigated the benefit of WATS3D used adjunctively to the combination of random and targeted forceps biopsy in the detection of esophageal dysplasia and BE. Investigators alternated taking forceps biopsies (FB) and WATS3D samples first. Of 12,899 patients enrolled, FB identified 88 cases of esophageal dysplasia, and WATS detected an additional 213 cases missed by FB. These 213 cases represented an absolute increase of 1.65%, increasing the yield from 0.68% to 2.33%. Adding WATS3D to FB increased the overall detection of esophageal dysplasia by 242%. Fewer than 61 patients needed to be tested with WATS to identify an additional case of esophageal dysplasia. The combination of random and targeted FB identified 1,684 cases of BE, and WATS detected an additional 2,570 BE cases. The absolute incremental yield of adding WATS3D to FB is 19.9%, increasing the rate of detection from 13.1% to 33%. Adding WATS3D to FB increased the overall detection of BE by 153%.

American College of Gastroenterology (ACG) stated, could not make a recommendation on the use of wide-area transepithelial sampling with computer-assisted 3-dimensional (WATS-3D) analysis in patients undergoing endoscopic surveillance of BE *(*Shaheen et al., 2022*).*American Gastroenterological Association (AGA) stated that WATS3D may be used as an adjunctive technique to sample the suspected or established Barrett's segment (in addition to the Seattle biopsy protocol), butfurther prospective studies directly comparing WATS-3D and Seattle protocol are needed to understand if WATS-3D sampling might be as or more effective. *(*Muthusamy et al, *2022))*
In their Clinical Practice Guidelines in Oncology for Esphageal and Esophagogastric Junction cancers, National Comprehensive Cancer Network stated that phase III randomized trials are needed to assess the utility and accuracy of WATS for detecting HGD/adenocarcinoma in patients with Barrett esophagus needs to be evaluated in larger phase III randomized trials. *(*NCCN, 2023)

In patients with known or suspected BE, American Society for Gastrointestinal Endoscopy (ASGE) suggests using WATS-3D in addition to Seattle protocol biopsy sampling compared with white-light endoscopy with Seattle protocol biopsy sampling a conditional recommendation based on low quality of evidence (ASGE, 2019).

Confocal laser endomicroscopy

Confocal fluorescent endomicroscopy, or confocal laser endomicroscopy is based on tissue illumination with a low-power laser with subsequent detection of the fluorescence light reflected from the tissue through a pinhole (ASGE, 2014). Confocal refers to the alignment of both illumination and collections systems in the same focal plane. Confocal endomicroscopy based on tissue fluorence uses a local and/or intravenous contrast agent and generates a high-quality image that may be comparable with traditional histological examination. Cellvizio® (Mauna Kea Technologies ,Newtown, PA) is a probe-based Confocal Laser Endomicroscopy (pCLE) device that is compatible with flexible video-endoscopes. The goal is to increase diagnostic yield while minimizing procedure-related risks and the costs of tissue acquisition and analysis.

Standard endoscopic evaluation of patients with Barrett's Esophagus (BE) is performed using high-definition, white light endoscopy (HD-WLE). Current guidelines, the Seattle Protocol, dictate random, 4-quadrant biopsies every 1 to 2 centimeters (cm) of BE length in addition to biopsies of suspicious areas. However, surveillance for esophageal precancer presents some challenges and there are drawbacks to HD-WLE. For example, random, 4-quadrant biopsies prompted by HD-WLE can miss up to half of cancers, dysplastic changes associated with BE are patchy and difficult to identify, changes may be uninterpretable when inflammation or ulceration is present, and the technique is associated with sampling error and low interobserver agreement (Hayes, 2016).
CLE illuminates the target area with a blue laser light (488 nanometers [nm] wavelength) following the topical application or intravenous (IV) administration of a fluorescent agent. Probe-based CLE (pCLE) with the Cellvizio 100 Series System and Cellvizio 100 Series System with Confocal Miniprobes (Mauna Kea Technologies) is performed using a small probe, which is advanced through the accessory channel of a standard endoscope. The device uses fixed laser power and a depth of imaging ranging from 0 to 130 micrometers (μm) for the gastrointestinal tract and from 55 to 65 μm for the ultra-high-definition probe. Images are acquired by placing the imaging aperture directly in contact with the esophageal mucosa; the images are then displayed on a screen similar to standard endoscopy. The recordings are often obtained using a transparent cap at the distal end of the endoscope, which provides stabilization. When a site is identified for biopsy, mild pressure is applied to the tissue with the confocal probe or an argon plasma coagulator and the resulting reddish mucosa guides subsequent acquisition of biopsy samples for histopathological examination and diagnosis. pCLE is performed in an outpatient setting by a board-certified gastroenterologist experienced in endoscopy. Patients undergo conscious sedation for the procedure and receive IV fluorescein to enhance the CLE images. pCLE is performed as an adjunct to standard HD-WLE. The additional procedure time adds approximately 5 to 20 minutes per patient.

Limitations of CLE systems include a limited viewing area and depth of view. Another issue is the standardization of systems for classifying lesions viewed with CLE devices. Gupta et al (2014) published a systematic review and meta-analysis of prospective studies comparing the accuracy of CLE plus targeted biopsy with standard 4-quadrant biopsy in patients with BE. In a meta-analysis of the diagnosis of HGD or esophageal adenocarcinoma, the pooled sensitivity was 68% (95% CI, 64% to 73%) and pooled specificity was 88% (95% CI, 87% to 89%). Leggett, et al. (2016) compared probe-based confocal endomicroscopy with volumetric endomicroscopy in ex vivo endoscopic mucosal resection specimens. The sensitivity, specificity, and diagnostic accuracy of probe-based confocal endomicroscopy for detection of BE dysplasia was 76% (95% confidence interval [CI], 59-88), 79% (95% CI, 53-92), and 77% (95% CI, 72-82), respectively. The use of volumetric laser endoscopy using a new algorithm showed a sensitivity of 86% (95% CI, 69-96), specificity of 88% (95% CI, 60-99), and diagnostic accuracy of 87% (95% CI, 86-88). Xiong et al (2016) published a meta-analysis of prospective studies evaluating the diagnostic accuracy of CLE in patients with BE, using histopathologic analysis as the criterion standard.(12) Studies were not required to compare CLE to standard 4-quadrant biopsy. Fourteen studies were included. In a pooled analysis seven studies (n=473 patients) reporting a per-patient analysis, the sensitivity of CLE for detecting neoplasia was 89% (95% CI, 82% to 94%) and the specificity was 83% (95% CI, 78% to 86%). The pooled positive and negative likelihood ratios were 6.53 (95% CI, 3.12 to 13.4) and 0.17 (95% CI, 0.11 to 0.29, respectively).

TissueCypher Barrett's Esophagus Assay is an artificial intelligence (AI) driven test that uses biomarkers, spatial biology, and an AI-driven risk classifier to identify a patient's five-year risk of progression to high-grade dysplasia (HGD) or esophageal adenocarcinoma (EAC) in patients with BE. The test characterizes molecular changes in BE tissue that precede dysplasia to identify candidates for eradication therapy for high-risk patients or reduced surveillance for low-risk patients (Davison et al., 2020; Castle Biosciences Inc., 2023a; Castle Biosciences Inc., 2023b). The test is intended for patients with a pathology diagnosis of nondysplastic BE (NDBE), indefinite for dysplasia (IND), or low-grade dysplasia (LGD) (Castle Biosciences Inc., 2023a). The test assesses 15 characteristics from 9 protein-based biomarkers and morphology in an esophagus tissue sample collected during an upper gastrointestinal endoscopy. The TissueCypher Image Analysis Platform is used to assess serial multichannel fluorescence of whole slide digital images. Algorithms combine characteristics of the biomarkers (e.g., fluorescence intensity) along with cell and tissue morphologic features (e.g., cell, nuclei, cytoplasm, plasma membrane) to assess the spatial relationship of biomarkers to each other and the tissue (Davison et al., 2020; Castle Biosciences Inc., 2023a; Castle Biosciences Inc., 2023e). The test calculates a risk score and reports a low, intermediate, or high risk of progression to HGD/EAC (Davison et al., 2020). There is no consensus among medical societies that supports TissueCypher. The ACG could not make a recommendation on the use of TissueCypher due to low sensitivity and specificity (Shaheen, 2022), while in their Clinical Practice Update on New Technology and Innovation for Surveillance and Screening in Barrett's Esophagus the AGA states that the assay may be of benefit for patients with nondysplastic BE (Muthusamy, 2022). Substantial uncertainty exists due to questions around test performance for identifying candidates for reduced surveillance;

evidence also suggests that the test may not reliably identify patients at low risk of progression who would be candidates for reduced surveillance (Critchley-Thorne et al., 2016; Critchley-Thorne et al., 2017; Davison et al., 2020; Frei et al., 2020). There is a lack of evidence demonstrating improved clinical outcomes with testing. Khoshiwal et al (2023) compared the risk stratification performance of the TissueCypher Barrett's Esophagus Test verus benchmarks of generalist and expert pathology. A total of 154 patients with BE (122 men), mean age 60.9 ± 9.8 years were studied. Twenty-four patients progressed to HGD/EAC within 5 years (median time of 1.7 years) and 130 did not progress to HGD/EAC within 5 years (median 7.8 years follow-up). The TSP-9 test demonstrated higher sensitivity (71% vs mean 63%, range 33%-88% across 30 pathologists), than the pathology review in detecting patients who progressed (P = .01186). However, currently no study has evaluated whether TissueCypher testing impacted patient clinical outcomes

V. CODING INFORMATION

Transoral Incisionless Fundoplication (TIF) for GERD

ICD-10 Codes:

K20.8x	Other esophagitis
K20.9x	Esophagitis, unspecified
K21.0x	Gastro-esophageal reflux disease with esophagitis
K21.9	Gastro-esophageal reflux disease without esophagitis

CPT/HCPCS Codes:

The following procedures are covered only for the gastroesophageal reflux disease (GERD) dx above:

43210	Esophagogastroduodenoscopy, flexible, transoral; with esophagogastric fundoplasty, partial or complete, includes duodenoscopy when performed (*when billed for EsophyX System)*
43257	Esophagogastroduodenoscopy, flexible, transoral; with delivery of thermal energy to the muscle of lower esophageal sphincter and/or gastric cardia, for treatment of gastroesophageal reflux disease *(when billed for Stretta System) Not covered for Priority Health Medicare*

The following procedures are not covered for the GERD diagnoses above:

43211	Esophagoscopy, flexible, transoral; with endoscopic mucosal resection
43229	Esophagoscopy, flexible, transoral; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)
43254	Esophagogastroduodenoscopy, flexible, transoral; with endoscopic mucosal resection
43270	Esophagogastroduodenoscopy, flexible, transoral; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)

Endoscopic Mucosal Resection, Thermal Ablation Treatment or Photodynamic Therapy for Barrett's Esophagus

ICD-10 Codes:

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

CPT/HCPCS Codes:

43211 Esophagoscopy, flexible, transoral; with endoscopic mucosal resection
43229 Esophagoscopy, flexible, transoral; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)
43254 Esophagogastroduodenoscopy, flexible, transoral; with endoscopic mucosal resection
43270 Esophagogastroduodenoscopy, flexible, transoral; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed)

96570 Photodynamic therapy by endoscopic application of light to ablate abnormal tissue via activation of photosensitive drug(s); first 30 minutes (List separately in addition to code for endoscopy or bronchoscopy procedures of lung and gastrointestinal tract)
96571 Photodynamic therapy by endoscopic application of light to ablate abnormal tissue via activation of photosensitive drug(s); each additional 15 minutes (List separately in addition to code for endoscopy or bronchoscopy procedures of lung and gastrointestinal tract)

J9600 Injection, porfimer sodium, 75 mg

Magnetic sphincter augmentation (MSA) - LINX device:

ICD-10 Codes:

K20.8x Other esophagitis
K20.9x Esophagitis, unspecified
K21.0x Gastro-esophageal reflux disease with esophagitis
K21.9 Gastro-esophageal reflux disease without esophagitis

CPT/HCPCS Codes:

43284 Laparoscopy, surgical, esophageal sphincter augmentation procedure, placement of sphincter augmentation device (i.e., magnetic band), including cruroplasty when performed. ***Prior Authorization Required***
43285 Removal of esophageal sphincter augmentation device. ***No Prior Authorization***

CPT/HCPCS Codes:

Diagnostic services:

91010 Esophageal motility (manometric study of the esophagus and/or gastroesophageal junction) study with interpretation and report;
91013 Esophageal motility (manometric study of the esophagus and/or gastroesophageal junction) study with interpretation and report; with

stimulation or perfusion (eg, stimulant, acid or alkali perfusion) (List separately in addition to code for primary procedure)
91020 Gastric motility (manometric) studies
91022 Duodenal motility (manometric) study
91030 Esophagus, acid perfusion (Bernstein) test for esophagitis
91034 Esophagus, gastroesophageal reflux test; with nasal catheter pH electrode(s) placement, recording, analysis and interpretation
91035 Esophagus, gastroesophageal reflux test; with mucosal attached telemetry pH electrode placement, recording, analysis and interpretation
91037 Esophageal function test, gastroesophageal reflux test with nasal catheter intraluminal impedance electrode(s) placement, recording, analysis and interpretation;
91038 Esophageal function test, gastroesophageal reflux test with nasal catheter intraluminal impedance electrode(s) placement, recording, analysis and interpretation; prolonged (greater than 1 hour, up to 24 hours)
91040 Esophageal balloon distension study, diagnostic, with provocation when performed

Prior Authorization Required:
0506U Gastroenterology (Barrett's esophagus), esophageal cells, DNA methylation analysis by next-generation sequencing of at least 89 differentially methylated genomic regions, algorithm reported as likelihood for Barrett's esophagus

The following procedures are not covered:
43201 Esophagoscopy, flexible, transoral; with directed submucosal injection(s), any substance (*when billed for Gatekeeper™ System, Enteryx™, PMMA beads, Duraspheres or other GERD /BE treatment not listed as covered)*
43206 Esophagoscopy, flexible, transoral; with optical endomicroscopy
43210 Esophagogastroduodenoscopy, flexible, transoral; with esophagogastric fundoplasty, partial or complete, includes duodenoscopy when performed *(when billed for EndoCinch™, Endoscopic Plication ™System*
43229 Esophagoscopy, flexible, transoral; with ablation of tumor(s), polyp(s), or other lesion(s) (includes pre- and post-dilation and guide wire passage, when performed) *(when billed for cryo or laser ablation techniques)*
43236 Esophagogastroduodenoscopy, flexible, transoral; with directed submucosal injection(s), any substance (*when billed for Gatekeeper™ System, Enteryx™, PMMA beads, Duraspheres or other GERD or BE treatment not listed as covered)*
43252 Esophagogastroduodenoscopy, flexible, transoral; with optical endomicroscopy
43254 Esophagogastroduodenoscopy, flexible, transoral; with endoscopic mucosal resection
0108U Gastroenterology (Barrett's esophagus), whole slide-digital imaging, including morphometric analysis, computer-assisted quantitative immunolabeling of 9 protein biomarkers (p16, AMACR, p53, CD68, COX-2, CD45RO, HIF1a, HER-2, K20) and morphology, formalin-fixed paraffin-embedded tissue, algorithm reported as risk of progression to high-grade dysplasia or cancer

WATS3D

WATS3D biopsy (CDx Diagnostics Inc.)

88104 Cytopathology, fluids, washings or brushings, except cervical or vaginal; smears with interpretation

88305 Level IV - Surgical pathology, gross and microscopic examination Abortion - spontaneous/missed Artery, biopsy Bone marrow, biopsy Bone exostosis Brain/meninges, other than for tumor resection Breast, biopsy, not requiring microscopic evaluation of surgical margins Breast, reduction mammoplasty Bronchus, biopsy Cell block, any source Cervix, biopsy Colon, biopsy Duodenum, biopsy Endocervix, curettings/biopsy Endometrium, curettings/biopsy Esophagus, biopsy Extremity, amputation, traumatic Fallopian tube, biopsy Fallopian tube, ectopic pregnancy Femoral head, fracture Fingers/toes, amputation, non-traumatic Gingiva/oral mucosa, biopsy Heart valve Joint, resection Kidney, biopsy Larynx, biopsy Leiomyoma(s), uterine myomectomy - without uterus Lip, biopsy/wedge resection Lung, transbronchial biopsy Lymph node, biopsy Muscle, biopsy Nasal mucosa, biopsy Nasopharynx/oropharynx, biopsy Nerve, biopsy Odontogenic/dental cyst Omentum, biopsy Ovary with or without tube, non-neoplastic Ovary, biopsy/wedge resection Parathyroid gland Peritoneum, biopsy Pituitary tumor Placenta, other than third trimester Pleura/pericardium - biopsy/tissue Polyp, cervical/endometrial Polyp, colorectal Polyp, stomach/small intestine Prostate, needle biopsy Prostate, TUR Salivary gland, biopsy Sinus, paranasal biopsy Skin, other than cyst/tag/debridement/plastic repair Small intestine, biopsy Soft tissue, other than tumor/mass/lipoma/debridement Spleen Stomach, biopsy Synovium Testis, other than tumor/biopsy/castration Thyroglossal duct/brachial cleft cyst Tongue, biopsy Tonsil, biopsy Trachea, biopsy Ureter, biopsy Urethra, biopsy Urinary bladder, biopsy Uterus, with or without tubes and ovaries, for prolapse Vagina, biopsy Vulva/labia, biopsy

88312 Special stain including interpretation and report; Group I for microorganisms (eg, acid fast, methenamine silver)

88361 Morphometric analysis, tumor immunohistochemistry (eg, Her-2/neu, estrogen receptor/progesterone receptor), quantitative or semiquantitative, per specimen, each single antibody stain procedure; using computer-assisted technology

WATS3D not covered for the following Barrett's esophagus diagnosis codes:

ICD-10 Codes:

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

Unlisted Codes: Explanatory notes must accompany claims billed with unlisted codes. Not covered if billed for GERD or BE for treatments listed in this policy as non-covered or not listed as covered.

E1399 Durable medical equipment, miscellaneous
L8499 Unlisted procedure for miscellaneous prosthetic services
43289 Unlisted laparoscopy procedure, esophagus

43499 Unlisted procedure, esophagus
43999 Unlisted procedure, stomach

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