FEP 2.01.38 Transesophageal Endoscopic Therapies for Gastroesophageal Reflux Disease

Effective Date: April 15, 2018

Related Policies:
2.01.80 Endoscopic Radiofrequency Ablation or Cryoablation for Barrett Esophagus
7.01.19 Injectable Bulking Agents for the Treatment of Urinary and Fecal Incontinence
7.01.137 Magnetic Esophageal Ring to Treat Gastroesophageal Reflux Disease

Transesophageal Endoscopic Therapies for Gastroesophageal Reflux Disease

Description

Transesophageal endoscopic therapies are being developed for the treatment of gastroesophageal reflux disease (GERD). A variety of procedures are being evaluated, including transesophageal (or transoral) incisionless fundoplication (TIF), application of radiofrequency energy, and injection/implantation of prosthetic devices or bulking agents.

FDA REGULATORY STATUS

In 2007, EsophyX® (EndoGastric Solutions, Redmond, WA) was cleared for marketing by FDA through the 510(k) process for full-thickness plication. In 2016, EsophyX® Z Device with SerosaFuse Fasteners was cleared for marketing by FDA through the 510(k) process (K160960) for use in transoral tissue approximation, full-thickness plication, ligation in the gastrointestinal tract, narrowing the gastroesophageal junction, and reduction of hiatal hernia of 2 cm or less in patients with symptomatic chronic GERD.3 In June 2017, EsophyX2 HD and the third-generation EsophyX Z Devices with SerosaFuse fasteners and accessories were cleared for marketing by FDA through the 510(k) process (K171307) for expanded indications, including patients who require and respond to pharmacologic therapy and in patients with hiatal hernias larger than 2 cm when a laparoscopic hiatal hernia repair reduces a hernia to 2 cm or less.4 FDA product code: ODE.

The Medigus SRS Endoscopic Stapling System (MUSE, Medigus) was cleared for marketing by FDA through the 510(k) process in 2012 (K120299) and 2014 (K132151). MUSE is intended for endoscopic placement of surgical staples in the soft tissue of the esophagus and stomach to create anterior partial fundoplication for treatment of symptomatic chronic GERD in patients who require and respond to pharmacologic therapy. FDA product code: ODE.

In 2000, the CSM Stretta® System was cleared for marketing by FDA through the 510(k) process for general use in the electrosurgical coagulation of tissue and was specifically intended for use in the treatment of GERD. Stretta® is currently manufactured by Mederi Therapeutics (Greenwich, CT). FDA product code: GEI.

Durasphere® is a bulking agent approved for treatment of urinary and fecal incontinence (see evidence review 7.01.19). Use of this product for esophageal reflux would be considered off-label use. The website of Carbon Medical Technologies states that the Durasphere® GR product is "intended to treat problems associated with GERD" but is considered an investigational device in the United States.

POLICY STATEMENT

Transoral incisionless fundoplication (ie, EsophyX®) is considered **investigational** as a treatment of gastroesophageal reflux disease.

Transesophageal radiofrequency to create submucosal thermal lesions of the gastroesophageal junction (ie, Stretta® procedure) is considered **investigational** as a treatment of gastroesophageal reflux disease.

Endoscopic submucosal implantation of a prosthesis or injection of a bulking agent (eg, polymethylmethacrylate beads, zirconium oxide spheres) is considered **investigationa**l as a treatment of gastroesophageal reflux disease.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

RATIONALE

Summary of Evidence

For individuals who have GERD and hiatal hernia of 2 cm or less that is not controlled by PPIs who receive TIF (eg, EsophyX), the evidence includes 2 RCTs comparing TIF with PPI therapy, nonrandomized studies comparing TIF with fundoplication, and case series with longer term follow-up. Relevant outcomes are symptoms, change in disease status, quality of life, medication use, and treatment-related morbidity. The highest quality RCT (RESPECT) was a sham-controlled together with PPI therapy while the other RCT (TEMPO) compared TIF with maximum PPI therapy. Both trials found a significant benefit of TIF on the primary outcome measure in about 65% of patients, but the sham-controlled trial found improvement in 45% of the sham-controlled group and no benefit on secondary subjective outcome measures. The nonblinded RCT found significant improvements in subjective measures but no difference in objective outcome measures when compared with PPI therapy. Together, these trials suggest a strong placebo effect of the surgery and a modest benefit of TIF in patients whose symptoms are not controlled by PPIs. For these patients, the most appropriate comparator is laparoscopic fundoplication. Studies comparing TIF with fundoplication have limitations that include earlier TIF procedures and unequal groups at baseline and are inadequate to determine relative efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have GERD and hiatal hernia of 2 cm or less that is controlled by PPIs who receive TIF (eg, EsophyX), the evidence includes 2 RCTs and observational studies with longer term follow-up. Relevant outcomes are symptoms, change in disease status, quality of life, medication use, and treatment-related morbidity. A sham-controlled trial found that the time to resume PPI therapy was longer following TIF and the remission rate was higher, indicating that TIF is more effective than no therapy. The nonblinded RCT found a benefit of TIF compared with continued PPI therapy for subjective measures, but not for the objective measures of pH normalization and esophagitis. These results raise questions about a possible placebo effect for the procedure. Also, observational studies have indicated a loss of treatment effectiveness over time. Adverse events associated with the procedure (eg, perforation) may be severe. At present, the available evidence does not support the use of this intervention in patients whose symptoms are adequately controlled by medical therapy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have GERD who receive endoscopic radiofrequency energy (eg, Stretta), the evidence includes 4 small RCTs, a nonrandomized comparative study, and observational studies with longer term follow-up. Relevant outcomes are symptoms, change in disease status, quality of life, medication use, and treatment-related morbidity. The RCTs reported some improvements in symptoms and quality of life following treatment with radiofrequency energy compared with sham controls. However, objective measures of GERD and a meta-analysis of these studies found no significant improvements in outcomes, raising questions about the mechanism of the symptom relief. Symptom relief is reported to be lower than after fundoplication, and reoperations greater. Larger RCTs with longer follow-up, preferably compared with fundoplication, are needed to define the risks and benefits of this procedure better. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have GERD who receive esophageal or bulking agents, the evidence includes an RCT and case series. Relevant outcomes are symptoms, change in disease status, quality of life, medication use, and treatment-related morbidity. The RCT for a single product was terminated early due to lack of efficacy, while other products have only case series to support use. High-quality data from large RCTs are needed to compare bulking procedures with both sham controls and with the currently accepted treatments for GERD (ie, drug therapy, laparoscopic fundoplication). Well-designed trials should use standardized outcome measures to examine whether subjective improvement (eg, discontinuation of medication therapy, GERD–Health-Related Quality of Life scores) is supported by objective improvement (eg, esophageal acid exposure). The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

American Society for Gastrointestinal Endoscopy

In 2015, the American Society for Gastrointestinal Endoscopy published guidelines on endoscopic procedures for gastroesophageal reflux disease (GERD).33 In their review of the EsophyX and Stretta procedures, the Society noted some positive findings but discrepancies between subjective and objective outcome measures or a lack of objective outcome measures in reported trials, concluding that these techniques represent “potentially new therapeutic indications for GI endoscopy”, but that prospective trials using objective measures of GERD as the primary end point could be useful in defining the clinical role of these procedures.

American College of Gastroenterology

Updated guidelines released by the American College of Gastroenterology in 2013 indicated that the use of current endoscopic therapy or transoral incisionless fundoplication (TIF) could not be recommended as an alternative to medical or traditional surgical therapy (conditional recommendation, moderate level of evidence).1 The guidelines also cited limited data on small numbers of subjects and short duration of follow-up.

Society of American Gastrointestinal and Endoscopic Surgeons

In 2017, the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) updated its evidence-based guidelines on endoluminal treatments for GERD.34 SAGES gave a strong recommendation based on moderate quality evidence that TIF with EsophyX can be performed with an acceptable safety risk in selected patients. SAGES concluded that EsophyX results in better control of GERD symptoms than proton pump inhibitor (PPI) treatment in the short term (6 months), and leads to similar improvement in objective GERD measures compared with PPIs. TIF appears to lose effectiveness during longer term follow-up and is associated with moderate patient satisfaction scores. SAGES found

no comparative, controlled trials between TIF and surgical fundoplication, but preliminary evidence suggested that the surgical fundoplication can be used safely after TIF failure.

SAGES gave a strong recommendation based on moderate quality evidence that Stretta is safe for adults and significantly improves health-related quality of life score, heartburn scores, the incidence of esophagitis, and esophageal acid exposure in patients with GERD. Stretta was found more effective than PPI, but less so than fundoplication.

American Society of General Surgeons

The American Society of General Surgeons (ASGS) issued a position statement on transoral fundoplication in 2011 stating that "ASGS supports the use of transoral fundoplication by trained General Surgeons for the treatment of symptomatic chronic gastroesophageal reflux disease (GERD) in patients who fail to achieve satisfactory response to a standard dose of Proton Pump Inhibitor (PPI) therapy or for those who wish to avoid the need for a lifetime of medication dependence."35

American Gastroenterological Association

In 2016, the American Gastroenterological Association issued a technology coverage statement on minimally invasive surgical options for GERD.36 Based on a literature review of 4 randomized controlled trials, a multicenter registry, and case series with longer term follow-up, the Association stated:

> "…evidence is sufficient to demonstrate sustainable improvement in health outcomes, symptom relief, decrease in PPI utilization and improvement in esophageal pH with transoral fundoplication. The selection criteria for transoral fundoplication includes GERD patients with BMI [body mass index] ≤ 35, hiatal hernia ≤ 2 cm, esophagitis LA [Los Angeles classification] grade A or B, Barrett's esophagus ≤ 2 cm, and absence of achalasia and esophageal ulcer. This option should be considered in patients not responding to PPI therapy (symptoms of regurgitation) who have documented objective evidence of GERD (pathologic acid exposure on pH testing (both off and on medication)) or esophagitis."

National Institute for Health and Care Excellence

In 2013, the National Institute for Health and Care Excellence (NICE) updated its guidance on endoscopic radiofrequency treatment for GERD, concluding: "The evidence on the safety of endoscopic radiofrequency ablation for gastro-esophageal reflux disease is adequate in the short and medium term, but there is uncertainty about longer term outcomes. With regard to efficacy, there is evidence of symptomatic relief, but objective evidence on reduction of reflux is inconclusive. Therefore, this procedure should only be used with special arrangements …."37 NICE noted "concern on the part of some specialists about the possibility that symptoms may improve as a result of denervation caused by the procedure; if that were the case then failure to recognize and treat reflux might lead to complications in the long term."

NICE issued guidance in 2011 on endoluminal gastroplication for GERD, concluding that "The evidence on endoluminal gastroplication for gastroesophageal reflux disease raises no major safety concerns. Evidence from a number of RCTs [randomized controlled trials] shows a degree of efficacy in terms of reduced medication requirement in the short term, but changes in other efficacy outcomes are inconsistent, and there is no good evidence of sustained improvement in esophageal pH measurements. Therefore, this procedure should only be used with special arrangements …."38

In 2017, NICE updated its guidance on bulking agents for GERD found that "Current evidence on the safety and efficacy of endoscopic injection of bulking agents for gastro-esophageal reflux disease does not appear adequate for this procedure to be used without special arrangements…."39 In 2016, NICE removed guidance on endoscopic bulking agents/hydrogel implants from guidelines on treatment for "dyspepsia and gastro-esophageal reflux" because the product had been withdrawn by the manufacturer.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

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POLICY HISTORY

Date	Action	Description
December 2011	New Policy	
March 2013	Update Policy	Policy updated with literature review; policy statement changed from investigational to not medically necessary for Stretta; deleted much of rationale information related to devices no longer available/ utilized.
March 2014	Update Policy	Policy with literature review, added references 4, 6, 10, 28, 29, and 36-38. No change to policy statement.
March 2015	Update Policy	Policy updated with literature review through October 8, 2014; Rationale revised; references 8, 11, and 17 added and some references removed; NDO Plicator, Endocinch, and Enteryx removed from policy.
March 2016	Update Policy	Policy updated with literature review through October 14, 2015; references 5-11, 14, 17, 19, 21, 28, and 30 added. Policy statement unchanged.
March 2017	Update Policy	Policy updated with literature review through August 31, 2016; reference 7 added. Policy statements unchanged.
March 2018	Update Policy	Policy updated with literature review through October 31, 2017; new references added. Policy statements unchanged.