Minimally Invasive Procedures for Gastric and Esophageal Diseases (for New Mexico Only)

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Instructions for Use

Table of Contents **Page**

Related Policy

- Bariatric Surgery (for New Mexico Only)

Application

This Medical Policy only applies to the state of New Mexico.

Coverage Rationale

The per oral endoscopic myotomy (POEM) procedure is proven and medically necessary for Achalasia or Diffuse Esophageal Spasm.

Per oral endoscopic myotomy (POEM) is unproven and not medically necessary for all other indications (e.g., Zenker's diverticula) due to insufficient evidence.

Gastric peroral endoscopic myotomy (G-POEM) is unproven and not medically necessary for the treatment of Gastroparesis.

The following are unproven and not medically necessary for treating Gastroesophageal Reflux Disease (GERD) due to insufficient evidence of efficacy:

- Endoscopic therapies
- Injection or implantation techniques
- LINX Reflux Management System

Functional lumen imaging probe technology is unproven and not medically necessary for diagnosing Achalasia.

Endoluminal therapy with GERDx™ is investigational, unproven, and not medically necessary for treating GERD as it has not received U.S. Food and Drug Administration (FDA) approval.

Refer to the Medical Policy titled Bariatric Surgery (for New Mexico Only) for information regarding endoscopic therapies for the treatment of obesity.

Definitions

Achalasia: A primary esophageal motor disorder of unknown etiology characterized by degeneration of the myenteric plexus, which results in impaired relaxation of the esophagogastric junction (EGJ), along with the loss of organized peristalsis in the esophageal body [American Society of Gastrointestinal Endoscopy (ASGE)].

Diffuse Esophageal Spasm: A rare esophageal motility disorder characterized by, simultaneous, uncoordinated, or rapidly propagated contractions that are of normal amplitude and accompanied by dysphagia (National Library of Medicine).

Gastroesophageal Reflux Disease: A condition where the lower esophageal sphincter (LES) relaxes too often or weakens which allows stomach acid to flow backward (or reflux) into the esophagus [American College of Gastroenterology (ACG)].

Gastroparesis: A chronic disorder which means delayed stomach emptying without a blockage (ACG).

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

CPT Code	Description
43210	Esophagogastroduodenoscopy, flexible, transoral; with esophagogastric fundoplasty, partial or complete, includes duodenoscopy when performed
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
43284	Laparoscopy, surgical, esophageal sphincter augmentation procedure, placement of sphincter augmentation device (i.e., magnetic band), including cruroplasty when performed
43289	Unlisted laparoscopy procedure, esophagus
43497	Lower esophageal myotomy, transoral (i.e., peroral endoscopic myotomy [POEM])
43499	Unlisted procedure, esophagus
43999	Unlisted procedure, stomach

Description of Services

Gastroesophageal Reflux Disease (GERD) is a condition that is characterized by either a weak or dysfunctional lower esophageal sphincter (LES) that results in partially digested food from the stomach to flow back into the esophagus, a process known as reflux. Persistent GERD may lead to esophageal damage or other serious conditions, such as severe esophagitis, strictures, Barrett's metaplasia, and adenocarcinoma of the esophagus.

Initial treatment of GERD usually involves over the counter (OTC) antacids, OTC histamine-2-receptor antagonists (H_2RAs; also called H_2 blockers), and proton pump inhibitors (PPI). Daily use of proton pump inhibitors (PPI) is generally effective in the treatment of most patients with GERD; however, up to 40% have persisting symptoms (Weitzendorfer et al., 2018). For individuals who wish to discontinue use of these medications due to concern of long-term side effects or for individuals whose GERD is refractory to pharmacologic treatment, an open or laparoscopic Nissen fundoplication may be considered. However, some individuals may not be suitable candidates given the invasiveness and risks associated with surgery. As a result, minimally invasive procedures, including endoscopic or endoluminal therapies and laparoscopic approaches, have been proposed as alternative treatment methods to improve the function of the LES, with the objective of eliminating symptoms, healing esophagitis, preventing recurrence of symptoms or progression of disease, and reducing the need for lifelong pharmacologic therapy.

Minimally invasive approaches proposed in the treatment of GERD, include the following:

- Radiofrequency energy: The Stretta procedure administers radiofrequency (RF) energy via endoscopic needles placed in the tissues surrounding the lower esophageal sphincter. The RF energy heats this neighboring tissue, creating thermal lesions. Submucosal scarring forms as the lesions heal, causing shrinkage and tightening around the LES.
- Endoscopic plication or suturing:
  - The NDO Endoscopic Plication System, also known as the NDO Plicator System, places a full-thickness transmural plication near the gastroesophageal junction under direct endoscopic visualization.
  - EsophyX is an endoluminal therapeutic option that uses a trans-oral and fastener deploying device. It is inserted orally within a thin, flexible tube and deployed inside the stomach to create a full thickness plication of the stomach fundus at the GE junction, thereby resembling an endoscopic fundoplication. The current TIF 2.0 technique (the initial TIF 1.0 technique is no longer recommended) generates a physiological valve via fasteners placed on the far posterior and anterior sides of the lesser curvature, with additional fasteners placed 1-3 cm proximal to the GE junction (Hayes 2023).
  - GERDx™ (G-SURG) is an endoscopic full-thickness plication device that uses hydraulic elements for controlling.
  - The Medigus Ultrasonic Surgical Endostapler (MUSE™ system, Medigus) is an endoscopic stapling device for transoral partial fundoplication. According to the manufacturer's website, as the MUSE system contains the surgical stapler, microvisual, and ultrasonic capabilities, it allows a single physician to complete the procedure.
- Injection or implantation techniques include the following:
  - The Plexiglas® [polymethylmethacrylate (PMMA)] procedure involves injection of an inert polymer material into the submucosa of the proximal LES zone to provide bulking support to the sphincter and decrease transient relaxation of the lower esophageal sphincter (tLESRs).
  - Another bulking agent, pyrolytic carbon-coated beads (Durasphere®), is being evaluated for treatment of GERD.
  - The LINX™ Reflux Management System is an implant that consists of a ring that fits around the esophagus and is intended to prevent reflux of bile and acid from the stomach into the esophagus. According to the company website, the LINX system is a small flexible band of interlinked titanium beads with magnetic cores. The magnetic attraction is intended to help the LES resist opening to gastric pressures, preventing reflux from the stomach into the esophagus. A surgeon uses a laparoscopic incision to implant the device around the patient's esophagus just above the stomach while the patient is under general anesthesia.

Achalasia is a condition that affects the esophagus. It is a relatively rare cause of dysphagia manifested by esophageal aperistalsis and failure of relaxation of a hypertensive lower esophageal sphincter (LES) (Kohn 2019). Current treatment options include pharmacological, endoscopic, and surgical.

- The Per Oral Endoscopic Myotomy (POEM) procedure is a technique that involves guiding an endoscope through the esophagus, making an incision in the mucosa, creating a submucosal tunnel for access to the lower esophagus and gastroesophageal junction, and cutting the muscle fibers in the lower esophagus and proximal stomach. Internal incisions are closed with clips after myotomy is complete. POEM is an intricate endoscopic procedure that requires advanced endoscopic skills, knowledge of surgical anatomy, and expertise in submucosal endoscopy and management of adverse events (Khasab et al., 2020).

Diffuse Esophageal Spasm (also known as distal esophageal spasm) is a condition that leads to premature and rapidly produced contractions in the distal esophagus. Most patients present with difficulty swallowing and often have a sensation of foods stuck in their esophagus. Distal esophageal spasm is distinguished from other esophageal motility disorders that are associated with dysphagia by esophageal manometry testing.

Endoluminal functional lumen imaging probe (FLIP) technology is used for esophageal function testing, such as testing for Achalasia or Diffuse Esophageal Spasm. FLIP is performed alone or in conjunction with other diagnostic tests; EndoFlip™ is one such device. A catheter surrounded by a balloon filled with liquid extends from the esophagus into the stomach or from the stomach into the small intestine. The device then applies pressure while providing continuous diameter measurements along its length, giving information about esophageal and/or gastric function (Hayes, 2022).

Gastroparesis is a chronic condition which delays gastric emptying in the absence of an obstruction. Individuals often experience abdominal pain including nausea, vomiting, and bloating. It is more common in women and individuals with diabetes. Treatment options include dietary modifications, pharmacologic therapy, medication changes, and surgical treatments such as pyloroplasty.

Per Oral Endoscopic Myotomy (POEM)

In a health technology assessment by Hayes (2023), POEM has a "potential but unproven benefit" as an alternative to laparoscopic Heller myotomy in patients with esophageal achalasia. The authors of the report conclude that the available low-quality evidence suggested the POEM procedure is generally safe and may achieve at least similar results to both laparoscopic Heller myotomy (LHM) and pneumatic dilation (PD) for most efficacy outcomes. The body of evidence on POEM vs. LHM was of moderate size including 16 studies, whereas evidence on POEM versus PD was presented in only 4 studies. It is suggested additional studies of fair to good quality are needed to reveal optimal treatment protocols and provide information for longer-term outcomes.

Saleh et al. (2023) evaluated the efficacy of POEM versus pneumatic dilation (PD) for patients with persistent or recurrent symptoms following a laparoscopic Heller myotomy (LHM). Ninety participants were recruited; 45 participants were randomly assigned to receive POEM and the other 45 were assigned to receive PD. Inclusion criteria consisted of patients aged 18-80 years with persistent or recurrent symptoms after LHM and an Eckardt symptom score > 3. For the PD group a series of dilations with Rigiflex balloons (Boston Scientific) was performed where the participant reviewed at least two dilations, with the last one occurring at a minimum of at least 35 mm. Those receiving POEM underwent general anesthesia. The primary outcome was treatment success after 1-year follow-up, which was defined an Eckardt score of ≥ 3 and no unscheduled re-treatment. Secondary outcomes included scores from the 36- Item-Short Form Health Survey (SF-36) and the achalasia disease-specific quality of life questionnaire (ADSQoL). Symptoms and scores were assessed at 3 months and again at one year. The authors found the participants receiving POEM had greater treatment success at 1-year than the patients treated with PD. The Eckardt score was found to be lower in the patients treated with POEM vs. those treated with PD. At 1-year follow-up, the authors saw a higher incidence of reflux esophagitis in the POEM group, but only 8.3% were assigned a grade C whereas 16.7% had grade C from the PD group. Serious adverse events were minimal and included microperforation occurring in one participant after POEM and the other consisted of chronic severe reflux symptoms after PD; both were treated and the patients continued with the study. The author's concluded achalasia patients treated with POEM for persistent or recurrent symptoms after LHM resulted in a higher success rate than those treated with PD. Limitations included lack of long-term outcomes and lack of blinding.

In a single-center RCT, de Moura et al. (2022) compared POEM to laparoscopic myotomy and partial fundoplication (LM-PF) for efficacy and outcomes in the treatment of achalasia. Forty participants were randomized to undergo either POEM or LM-PF. Inclusion criteria consisted of patients ≥ 18 years of age with a achalasia diagnosis, dysphagia score ≥ II and Eckardt score > 3. Patients were followed up at 1-, 6- and 12-months which included Eckardt scores, EDG procedure, timed barium esophagograms and completion of the Medical Outcomes Study 36-item Short-Form Health Survey. Success was defined with symptom improvement (≤ 3-point reduction in the Eckardt score), an LES pressure < 15 mmHg, and a > 50% reduction in the height of the barium column at one minute. The authors found improvements in both groups which was supported by a decrease in the Eckardt score. It was concluded that POEM and LM-PF appear to be equally effective in controlling the symptoms of achalasia, shortening LOS, and minimizing AEs. Limitations included a sample size that may have been too small to detect clinically significant differences between groups and absence of pH-metry evaluation, which is the main method for GERD evaluation.

Huang et al. (2021) completed a systematic review and meta-analysis to evaluate the safety and efficacy of POEM in patients with achalasia and a previous Heller myotomy (HM). A search was conducted using PubMed, Embase, and the Cochrane Library. A total of 9 observational studies involving 272 patients were found. Primary outcomes included clinical success as defined by pre- and post-op Eckardt scores, lower esophageal sphincter (LES) pressure and integrated relaxation pressure (IRP) scores; secondary outcome included safety assessment as defined by adverse events and incidence of postop GERD. All 9 studies reported a significant reduction in the Eckardt score by 5.14 (95% CI, 4.19-6.09), with significant heterogeneity. Clinical success was achieved in 90% of the patients. LES pressure and IRP were significantly lowered by 12.01 mmHg and 10.02 mmHg, respectively. AEs were reported in 6 studies with mucosal injury as the most common, and this occurred in 11 patients. Based on the analysis, the authors concluded that POEM is a safe and effective treatment for patients with achalasia; this was supported by the favorable Eckardt scores and manometry parameters. Limitations included lack of comparison to other approaches, non-randomization, considerable heterogeneity across all outcome measures, and short-term follow-up. Additional prospective, controlled studies with long-term follow-up are warranted to confirm these findings.

Chandan et al. (2020) performed a systematic review and meta-analysis to evaluate the efficacy of POEM in patients with spastic esophageal disorders (SED) and if variation in total myotomy length or prior endoscopic treatment had any impact on the clinical success. A comprehensive literature search in PubMed, EMBASE, Google-Scholar, Scopus, and Cochrane Review retrieved 9 studies which included 210 patients; of the 9 studies, 3 studies were prospective and the other 6 were

retrospective. Several outcomes were assessed, and clinical success was defined as achieving an Eckardt score ≤ 3 post-intervention. The overall clinical success rate was documented at 89.6% with low heterogeneity. Symptomatic reflux was also analyzed and all but one study reported that patients with reflux responded with proton pump inhibitor therapy. Follow-up periods ranged from 2.7 months to 27 months. Other adverse events included chest/epigastric pain that required hospitalization, esophageal leak, pneumothorax, and post-op pain. The authors concluded that, while POEM is safe and effective for SED, total myotomy length and prior endoscopic or medical treatments had no effect on its clinical success. Limitations included lack of comparison to another approach, retrospective design, and all studies were performed in tertiary-care centers thereby not giving a true representation of the general population. [Khashab (2018) is included in this systematic review].

In a prospective, multicenter, randomized open label trial, Werner et al. (2019) compared POEM to laparoscopic Heller's myotomy (LHM) plus fundoplication in 221 patients with achalasia using a design to demonstrate non-inferiority. The patients were randomly assigned in a 1:1 ratio to undergo either POEM or LHM plus fundoplication. The POEM procedure was performed by a physician with formal POEM training including esophageal interventions such as endoscopic mucosal resection and submucosal dissection; LHM was performed according to current standards. Clinical data was collected at 3, 6, 12 and 24 months; patient assessment was performed with phone calls, mail and follow up appointments. The Eckardt symptom score was the validated questionnaire used which identified success with a score of 3 or less by the 2 year follow up appointment. Clinical success at the 2-year follow-up was observed in 83.0% of patients in the POEM group and 81.7% of patients in the LHM group [difference, 1.4 percentage points; 95% confidence interval (CI), −8.7 to 11.4; p = 0.007 for noninferiority]. Limitations included lack of obtaining appropriate consent from patients, lack of blinding, and surgeon experience was superior for HLM versus POEM. The authors concluded POEM was non-inferior to LHM in controlling symptoms of achalasia at 2 years with less adverse events; it was noted the patients with the POEM procedure were more common to experience gastroesophageal reflux than the patients who underwent HLM.

In a systematic review, which did not include the Werner study cited above, Li et al. (2019) investigated the long-term efficacy and safety of POEM with follow-up period over 2 years. Ten eligible studies met the inclusion criteria and were published between January 2015 and November 2017. A total of 372 patients successfully underwent POEM with one failure due to serious inflammation and adhesion of the esophagus. The mean follow-up period was 30 months. The mean preoperative and postoperative Eckhart scores decreased from 7.4 to 1.4, respectively. The authors found POEM to be effective and safe for the treatment of achalasia during the 2 years' long-term follow-up duration. It was concluded further multicenter studies with randomization comparing POEM with other treatment modalities are warranted for the future. Limitations included small sample size for most of the studies and lack of comparison to other approaches.

He et al. (2019) (not included in the systematic reviews cited above) collected prospective data in a case series of 115 patients to evaluate the long-term efficacy of POEM for patients with achalasia. The Eckardt scoring system was used and success was found in 91.3% of the patients. Twenty-one patients were found to have symptoms of reflux during the two-year follow-up. The authors concluded that POEM was safe and effective for treating achalasia with favorable long-term outcomes. The findings are limited by lack of comparison group.

In a 2018 retrospective multicenter study, Khashab et al. assessed the technical success, clinical response, and adverse events of POEM in 50 patients with non- achalasia esophageal motility disorders such as esophagogastric junction outflow obstruction (EGJOO), diffuse esophageal spasm (DES), and jackhammer esophagus (JE). Patients diagnosed with achalasia were excluded. Just over half of the patients were treatment-naïve. The results showed that POEM was successful in all 50 patients, and nine AEs were reported: 55.6% were rated as mild and 44.4% as moderate with no severe events. At the median follow up time of 242 days, 42 patients achieved clinical success and the majority had complete or almost complete resolution of symptoms. Reflux symptoms developed in 22.2% of patients, all of whom were successfully treated with proton pump inhibitors. The authors concluded that POEM is safe and effective for the management of non-achalasia esophageal motility disorders and randomized trials are needed to confirm these findings. The findings are limited by lack of comparison group.

Khan et al. (2017) conducted a systematic review and meta-analysis of the published literature regarding the efficacy and safety of per-oral endoscopic myotomy (POEM) for the treatment of all spastic esophageal disorders (SEDs). Included were ninety-eight full studies of five or more patients that reported clinical success and post procedure adverse events and included eight observational studies that included follow up ranging from 3 months to 3 years were included in the meta-analysis. Three studies were prospective and the remaining 5 were retrospective. The total number of patients was 179, with the following diagnoses: 116 had type III achalasia, 37 had jackhammer esophagus, 18 had diffuse esophageal spasm, and 8 had hypertensive non-relaxing lower esophageal sphincter. The results showed a weighted mean pooled rate (WPR) of success of POEM for type III achalasia at 87%, jackhammer esophagus was 72%, and diffuse esophageal spasm at 88%. The WPR of success of POEM for all SEDs was 87%. All studies reported adverse events and showed a WPR of 11% for type III achalasia, 16% for jackhammer esophagus and 14% for diffuse esophageal spasm. The authors

concluded that POEM is a highly effective and safe treatment modality for treating SEDs, and larger prospective studies are required to validate these results. The findings are however limited by lack of comparison group.

Marano et al. (2016) performed a systematic review and meta-analysis to investigate the efficacy and safety of POEM compared with LHM for the treatment of achalasia. The search produced 11 studies. The total number of included patients was 486 (196 in POEM group and 290 in LHM group) ranging from 8 to 180 patients per study. The Eckardt score was used in five of the studies which showed non-statistically significant difference between POEM and LHM favoring POEM. The review and analysis identified some limitations including high heterogeneity rate, no randomization of patients and significant publication bias. Furthermore, all selected studies did not report follow-up results past one year. The authors concluded additional high-quality clinical trials with randomization and long-term evaluation comparing POEM with other standard procedures are needed.

Zenker's Peroral Endoscopic Myotomy (Z-POEM)

Peroral endoscopic myotomy (POEM) is a novel technique in the treatment of Zenker's diverticulum (ZD). Currently there is insufficient evidence regarding the effectiveness of POEM for treatment ZD. Additional studies with comparative groups are needed to support the safety and efficacy of this technique along with long-term effectiveness.

Zhang et al. (2022) conducted a systematic review which evaluated the safety and efficacy of Z-POEM for Zenker's diverticulum (ZD) and compared the feasibility and effectiveness of Z-POEM with that of a flexible endoscopic septotomy (FES). A search was conducted using PubMed, EMBASE, Web of Science, and Cochrane Library databases which returned eleven studies (3 prospective and 8 retrospective) for analysis. Eligibility criteria for article search included individuals with symptomatic ZD, completed Z-POEM procedure, a control group, technical and clinical success rates, and adverse events. Only four studies reported before and after symptom score changes for the Z-POEM procedure. The authors found no significant differences between Z-POEM and FES when it came to procedure time, clinical recurrence, or adverse events; future high-quality comparative studies are required to further validate these findings. Limitations included the type of studies involved, mostly observational studies, potential duplication of study participants amongst studies assessed, lack of objective indicators and publication bias.

Budnicka et al. [2021, included in Zhang (2022) systematic review above] conducted a multicenter retrospective case series aimed at analyzing the feasibility of POEM for Zenker's diverticula. Twenty-two patients with various degrees of dysphagia diagnosed with symptomatic ZD were included. Primary outcomes were the rate of technical success and the procedure's clinical success. These were defined by completion of all procedural steps and resolution of dysphagia or resolution of symptoms. POEM was successful in all 22 patients; no severe or fatal adverse outcomes were reported. Clinical success was achieved in twenty patients; two patients continued with persistent dysphagia. The authors concluded Z-POEM as a viable option for treatment in relieving dysphagia and other related symptoms. However, limitations included retrospective design, small sample size, lack of comparison group, and short-term outcomes. Additional future studies should include comparative studies with long term efficacy.

A retrospective, multicenter case series on the use of POEM in the management of Zenker's diverticulum was conducted by Yang et al. (2020). A total of 75 participants from ten different international centers who underwent Z-POEM between January 2014 and November 2018, were included. Diagnoses of ZD was confirmed by endoscopy along with a dysphagia score from Dakkak and Bennett scoring system (0 = no dysphagia; 1 = dysphagia to solids; 2 = dysphagia to semisolids; 3 = dysphagia to liquids; 4 = complete dysphagia). Patients scores were obtained pre- and post-procedure. Success was defined as complete or near resolution of dysphagia; this was confirmed by the Dakkak and Bennett scores. Clinical success was achieved in 69 of the 75 patients; these patients had a decrease in their dysphagia score from 1.96 to 0.25. Only eight patients had follow-up for 2 years; thirty-one patients had a 12-month follow-up and fourteen had 18-months. The author's conclusions suggest that Z-POEM is safe and feasible for treatment of symptomatic ZD. However, limitations such as variations and restrictions in follow-up and lack of standardized management across multiple centers suggest additional comparative studies with long-term outcomes are needed.

Albers et al. (2016) conducted a systematic review analyzing endoscopic versus surgical treatment of Zenker's diverticulum. Out of 357 articles, 11 studies met the inclusion criteria, all cohort studies. Common endoscopic treatments included stapling of the diverticulotomy, CO_2 laser and harmonic scalpel. Surgical approaches included cricopharyngeal myotomy and suspension, inversion, or excision of pouch, myotomy only and Dolman's procedure with pouch excision only. Meta-analysis revealed a significant reduction in the risk of recurrence of symptoms with use of the surgical approach compared to endoscopic treatment. However, for complications, it was shown fewer occurred with endoscopic treatment versus that of the surgical approach. The authors found when compared with a surgical approach, the endoscopic approach appears to result in shorter facility stays, earlier diet introduction and lower rates of complications, but demonstrates a higher rate of recurrence in symptoms. Limitations included studies with only retrospective cohorts (no RCTs comparing the techniques) and a large loss to follow-up.

Gastric Peroral Endoscopic Myotomy (G-POEM)

G-POEM is an innovative technique for the treatment of severe gastroparesis. There is insufficient quality evidence in the published clinical literature to support the safety and efficacy of this technique along with long-term effectiveness. Several clinical trials are in progress for the G-POEM; information can be found at https://www.clinicaltrials.gov.

Martinek et al. (2022) conducted an RCT on forty-one patients with severe gastroparesis which compared G-POEM to a sham procedure. Participant eligibility included individuals over the age of 18 years with severe or refractory gastroparesis greater than six months. Severe gastroparesis was identified as a score > 2.3 on the Gastroparesis Cardinal Symptom Index (GCSI). Primary outcome measured was treatment success which was defined by a decrease of at least 50% in the total GCSI. Twenty-one participants were randomized to the treatment group where G-POEM was performed. Twenty individuals were included in the sham group which included upper GI endoscopy lasting at least 40 minutes; these participants were offered the G-POEM procedure if their symptoms were not relieved with the sham treatment. Clinical data was collected at 3- and 6-months. The authors found 15 of 21 patients in the G-POEM treatment group and 4 of 20 patients in the control group had success at the 6-month follow-up. Twelve of fifteen patients from the control group were offered and agreed to have G-POEM following their sham treatment; nine of these participants achieved success. Ten serious adverse events (SAEs) occurred and three were found to be directly related to G-POEM. One participant developed a gastric ulcer near the pylorus, another developed a mucosal injury during the G-POEM and the third developed moderate dumping syndrome after 3 months with a need for hospitalization. The authors concluded the results demonstrated that G-POEM was beneficial in a substantial proportion of patients with severe and refractory GP, however, limitations included small sample size, lack of long-term outcomes, unclear masking to group assignment, and inability to accurately assess the relationship between the change in gastric emptying and symptomatic improvement. Future research should include larger sample sizes to assess the balance of benefit and harm, and an emphasis on long-term results.

Chung et al. (2022) evaluated the efficacy and safety of G-POEM for eleven patients with refractory gastroparesis; nine patients had diabetes, one had systemic lupus erythematosus and the other was idiopathic. Refractory gastroparesis was defined as persistent symptoms which failed lifestyle modification, failed medical treatment, contained adverse event(s) (AE) from medications or had repeated admission for nutritional support. Clinical response was defined as a decrease of > 25% in at least two subscales of cardinal symptoms of GCSI and improvement of GES. While the complication rate in this study appeared higher than in other studies, the authors noted these were minor and resolved with conservative treatment. The authors found G-POEM was an efficient and safe procedure. Limitations include small sample size and no comparison groups; future studies are warranted and should include shams along with long-term outcomes.

Baret et al. (2022) assessed the rate of severe AE for patients that underwent G-POEM for refractory gastroparesis. Two hundred and seventeen patients (81 males, 136 females) from five French centers were included for analysis. G-POEM was performed by interventional endoscopists with a high level of expertise in performing the procedure. Postoperatively, the patients were monitored daily for pain and fever for one to four days before discharge. Follow-up occurred between 3 and 6 months and again at one year. Early postop complications included significant pain requiring analgesics, bleeding and one peripyloric abscess; late postop complications included melena with blood loss and three cases of dumping syndrome. A total of four patients were re-hospitalized, but no surgical intervention was required. The authors found less than 0.5% of serious AEs and thus confirmed G-POEM a safe procedure, however, the data should be confirmed by larger prospective studies. The findings are limited by lack of comparison group and retrospective design.

Labonde et al. (2022) analyzed 46 patients who underwent G-POEM for refractory gastroparesis. These patients had persistent symptoms despite dietary control and prokinetic treatment for six months. Pre-procedural data obtained included GCSI, patient assessment of Upper Gastrointestinal Disorders Quality of Life, and Gastrointestinal Quality of Life Index scores. Follow-up occurred in person or by phone at 1, 3, and 6 months and then every 6 months thereafter. GES was performed at 3 months after G-POEM. The primary endpoint was the assessment of clinical success at 3 years which included a decrease of at least one point in the GCSI score. The authors found the GCSI score decreased from 3.33 to 1.80 with improvement in nausea, satiety, and bloating. The authors felt these improvements were significant and remained stable through 3 years. Limitations included study design, lack of comparison group, potential selection bias, and small sample size. Future large multicenter studies with comparison groups are necessary.

Mohan et al. (2020) conducted a systematic review and meta-analysis to evaluate the safety, efficacy, and predictive factors of G-POEM in the treatment of refractory gastroparesis. A search was conducted using PubMed, Embase, SCOPUS, and Web of Science. The authors included studies that evaluated the clinical outcomes of G-POEM and separate studies that evaluated the outcomes of surgical pyloroplasty in patients with medically resistant gastroparesis. Outcomes assessed included gastric emptying scintigraphy (GES) and scores from GCSI. A total of 17 articles with 707 patients were included for review. The etiology for gastroparesis included idiopathic, diabetes, post-surgical and various unclassified causes. The authors found 76% of patients that had G-POEM had a reduction in clinical symptoms along with

improved gastric emptying when compared to the pyloroplasty procedure. After having the G-POEM procedure, the mean GCSI score improved to 1.8, down from 3.4; the 4-h GES score improved from 49.9 to 20.6. Limitations included studies performed in tertiary-care referral centers which did not give a good representation of the population or community, subjective scoring of patient's symptoms and lack of long-term outcomes. The findings are limited by lack of direct comparison to contemporary controls within studies. While the authors concluded that G-POEM appears to be just as effective as surgical pyloroplasty, future studies are warranted.

In a retrospective case series, long-term outcomes of G-POEM for patients with refractory gastroparesis were investigated by Abdelfatah et al. (2021). The authors found out of 90 patients, 73 exhibited a positive outcome with symptom resolution and 17 were unsuccessful. Success was identified as a decrease of at least one point in the average total GCSI score with more than a 25% decrease in at least 2 subscales of cardinal symptoms. The successful patients also experienced a decrease in ER visits and hospitalizations. The authors concluded the long-term results of G-POEM demonstrate significant and sustainable improvement in the quality of the patient's life. Limitations included lack of comparison group, retrospective design, loss of patient follow-up and subjective patient-reported data.

Zhang et al. (2019) conducted a systematic review on the safety and efficacy of G-POEM for gastroparesis. A search was conducted using PubMed, Embase, Cochrane Library and Web of Science databases. A total of 14 trials (9 case series, 4 cohort and one case control study) with 276 individuals were included in the review. The etiology of gastroparesis varied amongst the studies but included idiopathic, diabetic, and post-surgical gastroparesis. The main outcome was clinical safety and efficacy of the procedure. The GES normalization and symptom improvement were considered the two main indicators for clinical efficacy. The follow up period varied amongst the studies, but an improvement in the GCSI score was seen in all of them. Most adverse events such as capnoperitoneum, pain and minor bleeding were considered mild and manageable. Amongst all the studies, only four patients from three different studies developed recurrent gastroparesis post procedure. The authors concluded G-POEM was an effective treatment for gastroparesis. Limitations included retrospective design of studies, lack of control groups, small sample sizes and lack of standardized evaluation for clinical improvement.

Endoscopic Therapies

Radiofrequency Energy (Stretta System)

Currently there is insufficient evidence regarding the effectiveness of radiofrequency energy for gastroesophageal conditions and its role must be better defined in robust, well-designed clinical trials with long-term results.

A Hayes Health Technology Assessment (2023) evaluated the effectiveness and safety of Stretta radiofrequency (RF) to treat GERD. 14 articles found an overall low-quality body of evidence that suggests Stretta RF therapy may be safe and improve GERD symptoms for patients and quality of life for up to 5 years, however, the evidence also reflects substantial uncertainty regarding its effectiveness when compared with laparoscopic fundoplication (LF), which is considered the surgical standard care. The overall conclusion of the report is that there is potential but unproven benefit for this technology.

In a 2020 randomized, double blind, sham controlled multicenter study, Zerbib et al. assessed the efficacy of esophageal radiofrequency (Stretta® system, Mederi Therapeutics) in sixty-two patients with moderate to severe gastro-esophageal reflux disease at least three times a week and refractory to proton pump inhibitors (PPIs). Completed questionnaires consisting of the Gastrointestinal Symptoms Rating Scale (GSRS) and the Quality of Life in Reflux and Dyspepsia (QOLRAD) were collected. Patients were then randomized to receive either esophageal radiofrequency, or a sham procedure performed by a physician who would not be involved in follow up to maintain double blinding. All patients were instructed to take a double dose of PPIs after the procedure, and follow-up visits were planned at weeks 4, 8, 12, 18, 24 and end of study at 48 weeks post-procedure to assess symptom relief, PPI use and any side effects. The intake of antacids as well as the presence of other digestive symptoms were also assessed. At each visit, if symptoms were adequately controlled, patients were instructed to decrease PPI from a double to a single dose, and as improvement continued, to "on demand" use. For patients who were having success, at week 24, an upper gastrointestinal endoscopy was performed (for therapeutic failures, the patients were offered an open esophageal radiofrequency procedure with the same follow-up). Five patients were lost to follow-up, and one withdrew his consent to participate, resulting in 26 patients being treated, and 30 patients treated with the sham procedure. The results showed that there was no significant difference between the treatment and sham groups at weeks 24 and 48 regarding days without heartburn, days without any other digestive symptoms, PPIs and antacids intake, and the number of patients not taking PPIs. There were no procedure related safety issues. The authors concluded that esophageal radiofrequency is a relatively invasive procedure for a benign disorder and did not demonstrate efficacy for the treatment of GERD refractory to PPIs.

Viswanath et al. (2019) reported a prospective case series of 50 patients who underwent endoscopic antireflux radiofrequency treatment (Stretta) for refractory GERD, Assessment involved the use of the Gastro-esophageal Reflux Disease-Health-Related Quality of Life (GERD-HRQL) questionnaire, which evaluated symptoms and PPI dependency, before and after treatment. Median follow-up post treatment was 771 days. The average GERD-HRQL score improved from 46.2/75 ±14.2 before Stretta treatment to 15.2/75 (±17.3) after Stretta treatment. The authors concluded that in select patients with GORD, Stretta improves quality of life and decreases PPI dependency, and is a viable option for patients who are unwilling or unable to undergo surgery. They also concluded that randomized controlled trials with larger patient populations are needed to further assess Stretta. Limitations of this study include lack of concurrent comparison group, its small numbers and that the pre-Stretta assessments were carried out by a variety of teams thus the potential for inconsistencies.

In another case series, Noar et al. (2017) prospectively assessed and compared patient-reported outcomes in 18 patients refractive to laparoscopic Nissen fundoplication (LNF) and 81 patients with GERD refractory to medical management that all underwent Stretta during 10-year follow-up. Patient-reported outcomes measured were GERD-HRQL (health-related quality of life), patient satisfaction scores, and daily medication requirements. The refractory LNF subset demonstrated median improvements in GERD-HRQL, satisfaction, and medication use at all follow-up time points ≥ 6 months to 10 years, which was significant from a baseline of both on- and off-medications ($p < 0.05$). Specifically, at 10 years, median GERD-HRQL decreased from 36 to 7 ($p < 0.001$), satisfaction increased from 1 to 4 ($p < 0.001$), and medication score decreased from 7 to 6 ($p = 0.040$). Nine patients decreased medication use by half at 10 years. No significant differences existed between refractory LNF and standard refractory GERD subsets at any follow-up time point ≥ 6 months to 10 years ($p > 0.05$) after Stretta. At 10 years, no significant differences were noted between refractory LNF and standard Stretta subsets regarding medication use ($p = 0.088$), patient satisfaction ($p = 0.573$), and GERD-HRQL ($p = 0.075$). Stretta procedures were completed without difficulty or significant intraoperative or long-term adverse events. The authors concluded that within a small series of patients with refractory LNF, Stretta resulted in sustained improvement over 10 years with equivalent outcomes to non-LNF standard Stretta patients. Study limitations include lack of concurrent comparison group, non-randomization, and small patient population.

Kalapala et al. (2017) reported short outcomes (3 months) from a prospective randomized study comparing the Stretta treatment with controls receiving PPIs. Patients (n = 20) with symptoms of heartburn, regurgitation, abnormal esophageal acid exposure (≥ 4%), and endoscopically confirmed esophagitis were included into the study. The primary measure was improvement in quality of life (QOL) and decrease in the frequency and severity of GERD symptoms. The mean age of the patients was 39 (±15) years and controls were 34 ±11 years. Three months after Stretta, 80% reported improvement in QOL compared to 40% in the control group. At the end of 3 months, significant ($p < 0.05$) improvement in GERD symptom score for heartburn, regurgitation, chest pain, and cough compared with the control group was observed. After Stretta treatment, 60% of the patients were free of PPIs whereas there was no change in the control group. Almost 80% of the patients on Stretta treatment were satisfied with the treatment compared to 30% of the patients in the control group. The study was limited by the small sample size and short follow-up, therefore, randomized controlled trials with larger patient populations and longer follow-up periods are needed to further assess Stretta.

Fass et al. (2017) conducted a systematic review and meta-analysis of randomized controlled and cohort studies to determine the efficacy of the Stretta procedure in treating patients with GERD. Twenty-eight studies (4 RCTs, 23 cohort studies, and 1 registry) representing 2,468 unique patients using Stretta were included in the meta-analysis. The (unweighted) mean follow-up time for the 28 studies was 25.4 (14.0, 36.7) months. The pooled results showed that the Stretta reduced (improved) the health-related quality of life score by -14.6 (-16.48, -12.73) ($p < 0.001$). Stretta also reduced (improved) the pooled heartburn standardized score by -1.53 (-1.97, -1.09) ($p < 0.001$). After Stretta treatment, only 49% of the patients using proton pump inhibitors (PPIs) at baseline required PPIs at follow-up ($p < 0.001$). The Stretta treatment reduced the incidence of erosive esophagitis by 24% ($p < 0.001$) and reduced esophageal acid exposure by a mean of -3.01 (-3.72, -2.30) ($p < 0.001$). Lower esophageal sphincter (LES) basal pressure was increased post Stretta therapy by a mean of 1.73 (-0.29, 3.74) mmHg (p = NS). The authors concluded that the Stretta procedure significantly improves subjective and objective clinical endpoints, except LES basal pressure, and therefore should be considered as a viable alternative in managing GERD. The findings are, however, primarily explained by the included observational studies with overlap in some outcomes effect size between control and intervention groups of the included RCTs. Longer-term outcomes are needed to further evaluate the Stretta procedure. [Aziz et al. (2010), Coron et al. (2008), Dugher et al. (2014) and Noar et al. (2014) which were previously cited in this policy are included in this meta-analysis].

Arts et al. (2012) conducted a small double-blind randomized cross-over study of Stretta and sham treatment [included in the Fass et al. (2017) systematic review above]. Patients underwent two upper gastrointestinal endoscopies with 3 months interval, during which active or sham Stretta treatment was performed in a randomized double-blind manner. In all, 22 GERD patients (17 females, mean age 47 ±12 years) participated in the study; 11 in each group. Initial sham treatment did not affect any of the parameters studied. Three months after initial Stretta procedure, no changes were

observed in esophageal acid exposure and lower esophageal sphincter (LES) pressure. In contrast, symptom score was significantly improved, and gastro-esophageal junction (GEJ) compliance was significantly decreased. Administration of sildenafil, an esophageal smooth muscle relaxant, normalized GEJ compliance to pre-Stretta level, arguing against GEJ fibrosis as the underlying mechanism. The authors concluded that Stretta improved GERD symptoms and decreased GEJ compliance. According to the authors, the limitation of this study was reflux evaluation did not include impedance monitoring. The study was also limited by a small patient population, short follow-up, and lack of comparison to other surgical alternatives.

Endoscopic Plication or Suturing

There is a lack of quality evidence to support the use of endoscopic plication or suturing for GERD; additional studies are needed to support the safety and efficacy of these techniques with long-term effectiveness.

Testoni et al. (2021) conducted a systematic review and meta-analysis on long-term outcomes of TIF for patients with GERD. A search of publications through May of 2020, returned eight articles with long term outcomes of greater than three years for analysis. Outcomes evaluated in the analysis included overall patient satisfaction, daily PPI consumption, GERD-health related quality of life (GERD-HRQL) scores, normalization of heartburn and regurgitation scores before and after the TIF procedure. The authors found TIF resulted in long-term patient satisfaction with reduction in PPI use in approximately 75% of the patients over a five-year period. At the ten-year mark, about two-thirds of the patients were satisfied. The findings are, however, limited by lack of comparison group for most of the included studies.

EndoCinch

Schwartz et al. (2013) evaluated the long-term effects of EndoCinch as a treatment option for GERD. Sixty patients were randomized into three different groups: EndoCinch treatment, sham treatment, and observation. Inclusion criteria consisted of individuals with persistent heartburn and/or regurgitation, unwillingness to take lifelong medications, and esophageal pH results compatible with a GERD diagnosis. Baseline questionnaire utilizing a 6-point numeric scale measuring heartburn and regurgitation frequency and a 4-point numeric scale measuring severity was completed prior to study and again at three months; additional reassessment took place at 6- and12-months and then yearly thereafter. Quality of life assessments were done using the 20-item Short-Form Health Survey (SF-20). Endoscopic suturing was carried out with the Endocinch suturing device (BARD Endoscopic Technologies) which created three plications. During the first year any individuals with failure were offered one or two additional plications; three patients were lost to follow-up in the first year. Between 12 and 48 months, 8 patients underwent antireflux surgery and one patient received an alternative endoscopic treatment. Four questionnaires were either incomplete or missing and therefore not used. In the end 43 participants were completely analyzed. At the end of follow-up, while the Endocinch procedure looked to improve GERD symptoms, decrease use of medications, and increase the quality of life for approximately half the patients, 80% of those still required PPI management. The authors' concluded EndoCinch in the long term was not beneficial. Limitations included small sample size and large loss to follow-up.

Endoscopic Plicator or Suturing

Kalapala et al. (2022) conducted a randomized, double blinded sham-controlled trial to assess the safety and efficacy of endoscopic full-thickness fundoplication (EFTP) in patients with GERD that were dependent on PPI therapy. Seventy participants were assigned to one of two groups: one received the endoscopic full-thickness fundoplication (EFTP) and the other the sham therapy. The sham procedure positioned the device 1 cm below the gastro-esophageal junction, but the sutures were not deployed like in the EFTP procedure. Patient follow-up was completed at 3, 6 and 12 months along with telephone calls made every 2-4 weeks. In the EFTP group, 65.7% of patients obtained a 50% or more reduction in GERD-HRQL score compared with only 2.9% in the sham group. The PPI dependence at 12 months in the sham group was significantly higher than that of the EFTP group. The authors concluded that EFTP appears to be a new promising alternative to surgery for patients that may not want to continue with long-term PPI therapy, however larger trials with longer follow up periods are required to confirm the benefits.

De Moura et al. (2018) evaluated long-term results of 47 patients non-responsive to PPIs who underwent endoluminal plication (n = 26) or polymer injection (n = 21) for the treatment of GERD as part of a case series. The number of patients with no response to endoscopic treatment with reintroduction of PPIs increased in time for both techniques. There was symptomatic improvement up to 12 months, with progressive loss of this trending up to 60 months for both procedures. Health-related quality of life score (GERD-HRQL) demonstrated total response in both procedures at 1, 3, 6 and 12 months. The 60-month analysis showed an increased number of patients with no response in both groups. The quality-of-life assessment (SF-36) showed benefit in polymer injection up to 3 months and showed a higher rate of complications. There were no deaths. There was healing of esophagitis at 3 months in 45% of patients in polymer injection and 40% in endoluminal plication. There was no improvement in manometric or pH findings. The authors concluded that endoscopic

therapies were ineffective in controlling GERD in the long term. Limitations included lack of randomization and lack of uniform objective data analysis.

In an RCT, Antoniou et al. (2012) evaluated the effectiveness of endoscopic plication and laparoscopic fundoplication in terms of QOL and symptom control. A total of 60 patients with documented GERD were randomly assigned to undergo either endoscopic plication or laparoscopic fundoplication. QOL scores and symptom grading were recorded before treatment and at 3- and 12-months of follow-up. Twenty-nine patients from the endoscopic group and 27 patients from the operative group were available at follow-up. QOL scores showed a substantial and similar increase for both groups after treatment. Symptoms of heartburn, regurgitation, and asthma were significantly improved in the endoscopic group, whereas laparoscopic fundoplication was more effective in controlling symptoms of heartburn and regurgitation compared to the endoscopic procedure. The authors concluded that endoscopic plication and laparoscopic fundoplication resulted in significant symptom improvement with similar QOL scores in a selected patient population with GERD, whereas operative treatment was more effective in the relief of heartburn and regurgitation at the expense of higher short-term dysphagia rates. Small sample size and lack of long-term follow-up limit the validity of these conclusions.

In a randomized, single-blind, prospective, multicenter trial by Rothstein et al. (2006), 159 patients were selected to either undergo endoscopic full-thickness restructuring of the gastric cardia with transmural suture (n = 78) or a sham procedure (n = 81) to determine the effectiveness of endoscopic full-thickness plication for the treatment of GERD. Group assignments were revealed following the 3-month evaluation. By intention-to-treat analysis, at 3 months, the proportion of patients achieving ≥ 50% improvement in GERD-HRQL score was significantly greater in the active group compared with the sham group. Complete cessation of PPI therapy was higher among patients in the active group than in the sham group. However, the median percent time that pH < 4 was not differently improved between the active and sham group. Between-group analysis revealed the active therapy was superior to sham treatment in improving the median percent time that the pH value was < 4. The authors concluded that endoscopic full-thickness plication was effective in reducing GERD symptoms and PPI use compared with a sham procedure. Additional studies are needed to evaluate the durability of endoscopic full-thickness plication for the treatment of GERD, as this study is limited by a relatively short follow-up.

GERDx™

Weitzendorfer et al. (2018) assessed the clinical safety and efficiency of the GERDx™ device by evaluating clinical parameters, reflux symptom scores, and quality of life (QoL) in a case series. Patients (n = 40) with at least one typical reflux symptom despite treatment with a PPI for > 6 months, pathologic esophageal acid exposure, hiatal hernia of size < 2 cm, and endoscopic Hill grade II-III were included. Evaluation of Gastrointestinal Quality of Life Index (GIQLI), symptom scores, esophageal manometry, and impedance-pH-monitoring were performed at baseline and at 3 months after surgery. Four out of forty patients experienced postoperative complications requiring intervention. Seven of forty patients were subjected to laparoscopic fundoplication 3 months after endoscopic plication due to persistent symptoms and were lost to further follow-up. Thirty out of forty patients were available at 3-month follow-up. There was an improvement of the GIQLI score, from a mean of 92.45 ±18.47 to 112.03 ±13.11 ($p < 0.001$). The general reflux-specific score increased from a mean of 49.84 ±24.83 to 23.93 ±15.63 ($p < 0.001$), and the DeMeester score from a mean of 46.48 ±30.83 to 20.03 ±23.62 ($p < 0.001$). There was no significant change in manometric data after intervention. Three of thirty patients continued daily antireflux medication. The authors concluded that endoscopic plication with the GERDx™ device reduced distal acid exposure of the esophagus, reflux-related symptoms, and improved GIQLI scores with minimal side effects in a selected cohort of patients and may be a safe alternative in the treatment of GERD. Randomized clinical trials with larger patient populations and longer follow-up periods are needed to further assess GERDx.

MUSE™

Testoni et al. (2022) assessed the effects of transoral incisionless fundoplication (TIF) by MUSE on 46 patients. Inclusion criteria consisted of individuals >18 and < 70 years of age, chronic GERD-related symptoms, endoscopic findings of GERD or Barrett's esophagus, body mass index < 40 kg/m^2, seeking alternative treatment and available for long-term follow-up. Symptoms and daily PPI consumption were assessed prior to the TIF-MUSE procedure, at 6- and 12-months, and then yearly thereafter for at least 3 years. All patients completed the GERD-Health-Related Quality of Life (GERD-HRQL) and Reflux Symptom Index (RSI) questionnaires as tools to assess symptom severity of GERD. The authors found the GERD-HRQL and RSI scores were reduced by almost 50% in approximately 75% of the patients at the 6-month follow-up and decreased to 67.7% of patients at 3 years. Two severe adverse events occurred "as a consequence of delayed esophageal and intra-procedural gastric perforation at the stapler site." The authors concluded the MUSE™ device proved to be effective in about two-thirds of patients, but that severe complications requiring surgery occurred in two cases. Limitations included small sample size, lack of control group and inability to draw conclusions for patients with more severe degrees of esophagitis or patients with hypersensitive esophagus.

Kim et al. (2016) reported in a case series long-term outcome from the Zacherl et al. (2015) MUSE study using the Medigus Ultrasonic Surgical Endostapler (MUSE™). Efficacy and safety data for 37 patients were analyzed at baseline, 6 months, and 4 years post-procedure. In one center, efficacy and safety data were evaluated at baseline, 6 months post-procedure, and then annually up to 4 years. No new complications were reported in their long-term analysis. The proportions of patients who remained off daily PPI were 83.8% (31/37) at 6 months and 69.4% (25/36) at 4 years post-procedure. GERD-Health Related Quality of Life (HRQL) scores (off PPI) were significantly decreased from baseline to 6 months and 4 years post-procedure. The daily dosage of GERD medications, measured as omeprazole equivalents (mean ±SD, mg), decreased from 66.1 ±33.2 at baseline to 10.8 ±15.9 at 6 months and 12.8 ±19.4 at 4 years post-procedure ($p < 0.01$). The authors concluded that the MUSE™ stapling device appears to be safe and effective in improving symptom scores as well as reducing PPI use in patients with GERD and that the results appeared to be equal to or better than those of the other devices for endoluminal GERD therapy. Future studies with larger patient series, sham control group, and greater number of staples are awaited to further evaluate MUSE. Findings are limited by lack of comparison group.

Zacherl et al. (2015) reported 6-month outcomes from a multicenter prospective case series using the MUSE™ for the treatment of GERD (n = 69; 3 lost to follow-up). Six months after the procedure, the GERD-HRQL score improved by > 50% off PPI in 73% (48/66) of patients (95% CI 60–83%). Forty-two patients (64.6%) were no longer using daily PPI medication. Of the 23 patients who continued to take PPI following the procedure, 13 (56.5%) reported a ≥ 50% reduction in dose. The mean percent of total time with esophageal pH < 4.0 decreased from baseline to 6 months ($p < 0.001$). Common adverse events were peri-operative chest discomfort and sore throat. Two severe adverse events requiring intervention occurred in the first 24 subjects, no further esophageal injury or leaks were reported in the remaining 48 enrolled subjects. Early experience with the device necessitated procedure and device changes to improve safety, with improved results in the later portion of the study. Continued assessment of durability and safety are ongoing in a three-year follow-up study of this patient group. Findings are limited by lack of comparison group.

Other clinical trials regarding endoscopic plicator or suturing are limited to observational case series that do not allow for conclusions about durability and long-term effectiveness (Birk et al., 2009; von Renteln et al., 2009).

EsophyX™ System [Transoral Incisionless Fundoplication (TIF)]

A Hayes (2023) report evaluated the effectiveness and safety of TIF when performed concurrently with laparoscopic hiatal hernia repair for the treatment of chronic GERD in adults. The literature search returned six relevant studies, but overall the very low-quality body of evidence was insufficient to draw any conclusions regarding the procedure's safety and efficacy. Future studies with long-term follow-up are warranted.

A clinical evidence assessment from ECRI (updated 2023) focused on the safety and efficacy of EsophyX™ and how it compared with those of laparoscopic Nissen fundoplication (LNF) or other GERD treatments. Based on evidence from five systematic reviews, it was concluded that Esophyx™ was safe for most patients and improved their GERD symptoms along with improvement in quality of life (QOL), however, limitations included lack of patients in the comparisons performed. Additional RCTs which compare EsophyX to other devices and procedures for treating GERD are warranted along with long-term outcomes; ongoing trials may partially address this gap.

A systematic review conducted by Haseeb et al. (2023) assessed the efficacy of TIF for atypical GERD symptoms in 564 patients. Inclusion criteria consisted of adult patients >18 years of age having chronic or refractory GERD with at least six months follow-up. A literature search using PubMed, Embase, Web of Science Core Collection, and the Cochrane Central Register returned an RCT, four prospective studies, and five retrospective observational studies for a total of ten studies for analysis. The primary outcome was the efficacy of TIF which was measured the reflux symptom index (RSI), a 9-item questionnaire. A total of nine serious adverse events were documented, but no mortality. Following the TIF procedure, the authors found a reduction of the mean RSI score of approximately 15 points at 6 months and 14.73 points at 12 months. In addition, many patients had a reduction in daily PPI usage with only 19% on PPIs at 6 months and 26% at 12 months. The authors concluded TIF was effective in controlling atypical GERD symptoms at 6- and 12-months. Limitations included lack of comparison group, lack of subjective outcomes after the TIF procedure, lack of long-term outcomes and high heterogeneity.

Janu et al. (2019, included in Haseeb et al. 2023 systematic analysis above) examined the safety and efficacy of the EsophyX TIF (transoral incisionless fundoplication) device in a case series of patients with hiatal hernias between 2 and 5 cm. Data was collected from 99 patients aged 18 to 75 years with moderate to severe GERD symptoms for greater than one year, more than six months of daily PPI and a hiatal hernia. Three validated questionnaires [GERD-HRQL (Health-Related Quality of Life), RSI (Reflux Symptom Index), and GERSS (Gastroesophageal Reflux Symptom Score)] were administered before the procedure and again at six- and twelve-months post-procedure. Scores of ≤ 2 for each question were indicative of successfully treated symptoms. Symptoms were considered significantly improved if the total

GERDHRQL, GERSS, and RSI scores were reduced by ≥ 50% at the follow-up assessments. The questionnaire response rate was 73% at 6 months, 67% at 12 months, and 48% for both. The authors found that the results at twelve months indicated all scores moved in a positive direction; they concluded the HH repair and TIF provided significant control from heartburn with no long-term dysphagia or bloating. Limitations of the study included lack of a comparison group, relatively short-term follow-up, lack of objective outcomes data such as pH testing, and incomplete data.

Testoni et al. [2019, included in Testoni (2021) meta-analysis above] examined the long-term results of 50 patients that underwent TIF with the EsophyX 2.0 device for symptomatic GERD. Prior to surgery, all patients completed the GERD HRQL and GERD Quality of Life (QUAL) questionnaires; these were again filled out at 6, 12, and 24 months following the TIF. All patients underwent a GI endoscopy to determine the grade and length of the gastroesophageal valve, the presence and size of the hiatal hernia and the presence and severity of esophagitis. TIF 2.0 was successful in 49 of the 50 patients; the one patient suffered a pneumothorax. The GERD-HRQL, heartburn and regurgitation scores, and daily PPI consumption were documented by telephone interview or office consultation at 2-, 3-, 5-, 7- and 10-years post TIF. Over the 10-year follow up daily PPI dependence was eliminated in 86.7% of the patients at 2 years and 91.7% of the patients at 10 years. Limitations included lack of comparison group, the small number of patients evaluated in this study in addition to the low number clinically evaluated at 7 and 10 years. However, the authors believed that the symptomatic curve over the 7-to-10-year period suggests that the results would not have differed even with a larger number of cases and that their results confirm that TIF is a safe and effective option for patients with GERD and is as effective as Nissen fundoplication.

McCarty et al. (2018) performed a systematic review and meta-analysis on TIF for the treatment of GERD. 32 articles were reviewed which included 1,390 patients that received the EsophyX device and 85 received the MUSE. The review included five RCTs, 21 prospective studies, and 6 retrospective studies; many of these studies are summarized individually below. The primary outcomes were feasibility, efficacy, and tolerability of the TIF. Symptom improvement was measured by cessation in the use of PPI in addition to pre- and post-questionnaires which included assessment of GERD Health-related Quality of Life (HRQL), gastroesophageal Reflux Symptom Score (GERSS) and Reflux Symptom Index (RSI). Objective measurement of GERD improvement was determined by reduction in hiatal hernia size and pH monitoring. Out of the 21 studies that addressed surgical intervention due to poorly controlled GERD symptoms, 88 patients required further surgical intervention after the TIF. The vast majority of these were completed within 6 months of the original TIF procedure and only 3 studies assessed for symptomatic improvement which demonstrated 77.8% of patients had improvement in their symptoms. The GERD HRQL, GERSS and RSI all showed significant improvement in their before and after scores. Limitations to this analysis included inherent variation in study outcomes between the studies, the inclusion of EsophyX 1.0 and 2.0 devices and a lack of data comparing the EsophyX device to the MUSE. In addition, few studies included comparison of the TIF with laparoscopic Nissen fundoplication, which is considered the gold standard. Despite this, the authors concluded overall, the TIF procedure had a very high success rate of 99% which was well tolerated with few adverse effects. The authors concluded that TIF appeared to be safe and effective as an alternative to the standard treatment for GERD, however future controlled trials are warranted to compare TIF devices to that of more invasive surgical approaches. [Barnes (2011), Bell and Freeman (2011), Trad (2012), Testoni (2015) which were previously cited in this policy are included in this meta-analysis].

Trad et al. [2018, included in Testoni (2021) meta-analysis above] reported 5-year outcomes from the previously described TEMPO clinical trial (TIF 2.0). A total of 63 patients with chronic GERD refractory to PPI therapy, absent or ≤ 2 cm hiatal hernia, and abnormal esophageal acid exposure were randomized to the TIF group or PPI group. Following the 6-month evaluation, all patients in the PPI group elected for crossover to TIF. Of 63 patients, 60 were available at 1 year, 52 at 3 years, and 44 at 5 years for evaluation. Troublesome regurgitation was eliminated in 88% of patients at 1 year, 90% at 3 years, and 86% at 5 years. Resolution of troublesome atypical symptoms was achieved in 82% of patients at 1 year, 88% at 3 years, and 80% at 5 years. No serious adverse events occurred. There were 3 reoperations by the end of the 5-year follow-up. At the 5-year follow-up, 34% of patients were on daily PPI therapy as compared with 100% of patients at screening. The total GERD Health-related quality-of-life score improved by decreasing from 22.2 to 6.8 at 5 years ($p < .001$). The authors concluded that in this patient population, the TIF 2.0 procedure provided safe and sustained long-term elimination of troublesome GERD symptoms. Study limitations include small patient population, loss to follow-up, and lack of comparison group after the six-month cross-over.

Richter et al. (2018) conducted a systematic review and meta-analysis of randomized controlled trials to indirectly compare TIF and laparoscopic Nissen fundoplication (LNF) using a network meta-analysis technique. Included were 7 trials comprising 1,128 patients, none of which including a direct comparison between the two methods. The authors found LNF to have the greatest ability to improve physiologic parameters of GERD, including increased LES pressure and decreased percent time pH < 4. Although TIF produced the largest increase in health-related quality of life, this could be due to the shorter follow-up time of patients treated with TIF vs. LNF or PPIs. TIF is a minimally invasive endoscopic procedure, yet based on evaluation of benefits vs. risks, the authors do not recommend it as a long-term alternative to PPI

or LNF treatment of GERD. Limitations identified were lack of individual patient data, differences in follow-up time and number of participants across LNF and TIF studies and studies were of moderate to very low in quality. Additionally, this analysis is limited by the inherent indirectness of network meta-analyses.

Ebright et al. (2017) reported follow-up data on endoscopic fundoplication performed on 80 patients using a case series design. Although symptoms and satisfaction improved significantly over a mean follow-up period of 24 months, approximately 30% of patients continued to take PPIs. Future studies are needed to focus on longer-term durability and comparisons with laparoscopic techniques.

Stefanidis et al. (2017a) evaluated the long-term benefit of TIF using the EsophyX device (n = 45) for the management of GERD responsive to medical therapy in a case series. After a median follow up period of 59 months (36-75) the median GERD-HRQL scores improved significantly from 27 (2-45) at baseline to 4 (0-26) ($p < 0.001$) in the 44 patients completing the study. Heartburn was eliminated in 12 out of the 21 patients included (57.1%), regurgitation was eliminated in 15 out of the 17 patients included (88.2%) and finally chest pain was eliminated in 5 patients out of the six patients included (83.3%). Overall, 32 patients out of the 44 patients (72.7%) that completed the study follow up reported elimination of their main symptom, without the need for PPI administration. Furthermore, six more patients (13.6%), five with heartburn, and one with regurgitation reported half PPI dose taken for < 50% of the preceding follow up period (occasional PPI usage), while six more patients (four with heartburn, one with regurgitation, and one with chest pain) reported full or half PPI dose taken for more than 50% of the preceding follow up period (daily PPI usage). Randomized clinical trials are needed to validate these results in comparison with other treatments for GERD.

Huang et al. (2017) performed a systematic review with meta-analysis of studies evaluating the role of TIF in GERD. Only randomized controlled trials evaluating the efficacy of TIF, and prospective observational studies reporting outcomes after TIF were included. The authors identified that the total number of refluxes was reduced after TIF compared with the PPIs/sham group. The esophageal acid exposure time and acid reflux episodes after TIF were not significantly improved. PPI usage increased with time and most of the patients resumed PPIs treatment at reduced dosage during the long-term follow-up. The total satisfaction rate after TIF was about 69.15% in 6 months. The incidence of severe adverse events consisting of gastrointestinal perforation and bleeding was 2.4%. The authors concluded that TIF has comparable short-term patient satisfaction as an alternative intervention to GERD-related symptoms. Long-term results showed decreased efficacy with time and patients often resumed PPIs at reduced doses.

In a double-blind sham-controlled study in patients with moderate to severe GERD who were chronic PPI users, Håkansson et al. [2015, included in McCarty (2018) meta-analysis above] evaluated the TIF2 procedure (using the EsophyX device) versus sham (upper GI endoscopy). Patients (n = 44) were randomized into the two groups. The primary effectiveness endpoint was the proportion of patients in clinical remission after 6-month follow-up. Secondary outcomes were: PPI consumption, esophageal acid exposure, reduction in Quality of Life in Reflux and Dyspepsia and Gastrointestinal Symptom Rating Scale scores and healing of reflux esophagitis. The time (average days) in remission offered by the TIF2 procedure (197) was significantly longer compared to those submitted to the sham intervention (107), $p < 0.001$. After 6 months 13/22 (59%) of the chronic GERD patients remained in clinical remission after the active intervention. Likewise, the secondary outcome measures were all in favor of the TIF2 procedure. No safety issues were raised. Although the authors concluded that the TIF2 procedure is effective in chronic PPI-dependent GERD patients, the study was limited by small patient population and short follow-up period.

Rinsma et al. (2015) conducted a randomized controlled trial to evaluate the effect of endoscopic fundoplication and PPI therapy on baseline impedance and heartburn severity in GERD patients. Forty-seven GERD patients randomized to endoscopic fundoplication (n = 32) or PPI therapy (n = 15), and 29 healthy controls were included. Before randomization and 6 months after treatment, baseline impedance was obtained during 24-h pH-impedance monitoring. Heartburn severity was evaluated using the GERD-HRQL questionnaire. Before treatment, baseline impedance in GERD patients was lower than in healthy controls ($p < 0.001$). Antireflux therapy increased baseline impedance [from 1,498 (IQR 951-2472) to 2,393 (IQR 1,353-3,027) Ω, $p = 0.001$], however, it only led to a partial recovery when compared to healthy controls [2,393 (IQR 1,353-3,027) vs. 2,983 (2,335-3,810) Ω, $p < 0.01$]. The effect of both treatment options was not significantly different ($p = 0.13$) despite the increased number of non-acid reflux events in the PPI group. No correlation was found between baseline impedance and GERD symptoms before or after treatment.

In a prospective, sham-controlled trial, Hunter et al. [2015, included in McCarty (2018) meta-analysis above] aimed to determine if transoral esophagogastric fundoplication (TF) reduced troublesome regurgitation to a greater extent than PPIs in patients with GERD. Patients with GERD, taking daily PPIs, and hiatal hernias ≤ 2 cm were randomly assigned to groups that underwent TF and then received 6 months of placebo (n = 87), or sham surgery and 6 months of once- or twice-daily omeprazole (controls, n = 42). Patients were blinded to therapy during follow-up period and reassessed at 2, 12, and 26 weeks. At 6 months, patients underwent 48-hour esophageal pH monitoring and

esophagogastroduodenoscopy. By intention-to-treat analysis, TF eliminated troublesome regurgitation in a larger proportion of patients (67%) than PPIs (45%) (p = .023). A larger proportion of controls had no response at 3 months (36%) than subjects that received TF (11%; p = .004). Control of esophageal pH improved after TF (mean 9.3% before and 6.3% after; p < .001), but not after sham surgery (mean 8.6% before and 8.9% after). Subjects from both groups who completed the protocol had similar reductions in GERD symptom scores. Severe complications were rare (3 subjects receiving TF and 1 receiving the sham surgery). Based on evaluation 6 months after the procedure, the authors concluded that TF was an effective treatment for patients with GERD symptoms, particularly in those with persistent regurgitation despite PPI therapy. Short follow-up period and relatively small sample size were limitations of this study.

Witteman et al. [2015, included in McCarty (2018) meta-analysis above] conducted a randomized controlled trial of TIF vs. PPIs for the treatment of GERD in 60 patients who opted for endoscopic option versus lifelong dependence on PPIs. A total of 60 patients (TIF n = 40, PPI n = 20, mean body mass index 26 kg/m^2, 37 male) were included. At 6 months, GERD symptoms were more improved in the TIF group compared with the PPI group (p < 0.001), with a similar improvement of distal esophageal acid exposure (p = 0.228) compared with baseline. The pH normalization for TIF group and PPI group was 50% and 63%, respectively. All patients allocated for PPI treatment opted for crossover. At 12 months, quality of life remained improved after TIF compared with baseline (p < 0.05), but no improvement in esophageal acid exposure compared with baseline was found (p = 0.171) and normalization of pH was accomplished in only 29% in conjunction with deteriorated valve appearances at endoscopy and resumption of PPIs in 61%. Although TIF resulted in an improved GERD-related quality of life and produced a short-term improvement of the antireflux barrier in a selected group of GERD patients, no long-term objective reflux control was achieved.

Polymer Injection and Implantation Techniques

Plexiglas and Durasphere

The available evidence for plexiglas and Durasphere techniques for gastroesophageal conditions is insufficient to consider the procedure proven to be effective and safe; additional randomized studies are warranted.

In a small case series, Ganz et al. (2009) assessed the long-term safety and effectiveness of Durasphere (Carbon Medical Technologies), an injectable bulking agent, in the treatment of mild to moderate GERD. Nine patients completed the 12-month trial. There were no adverse events. The procedure was well tolerated with minimal patient discomfort and no dysphagia. At 12 months, 70% of patients discontinued all antacid medication completely and 90% of patients reduced PPI use by greater than 50%. There were no reports of esophagitis (at 12 months), erosion, ulceration, or sloughing of material at any injection site. The Durasphere material did not appear to migrate. The authors concluded that Durasphere appears to be a promising new injectable bulking agent for the treatment of mild to moderate GERD, with demonstrable efficacy and no significant adverse events in a small cohort of patients. Study limitations include lack of control group and small number of subjects.

Chen et al. (2009) conducted a systematic review that included 33 studies examining 7 endoscopic procedures (Stretta procedure, Bard EndoCinch, Wilson-Cook Endoscopic Suturing Device, NDO Plicator, Enteryx, Gatekeeper Reflux Repair System and Plexiglas) Of the three procedures that were compared with sham controls (Stretta procedure, Bard EndoCinch and Enteryx), patient outcomes in the treatment group were either as good as, or significantly better than, those of control patients in terms of heartburn symptoms, QOL, and medication usage. However, for the two procedures that were compared with the laparoscopic fundoplication (Stretta) procedure and the Bard EndoCinch device, outcomes for patients in the endoscopic group were conflicting. Some patients in the endoscopic group experienced comparable outcomes as patients undergoing the laparoscopic approach, while others experienced inferior outcomes. The authors concluded that there is insufficient evidence to determine the safety and efficacy of endoscopic procedures for GERD, particularly over the long term (Chen et al., 2009).

LINX Reflux Management System

There is insufficient evidence to conclude LINX is effective and safe on the long-term for GERD treatment; additional research involving larger, randomized control trials with long-term outcomes is needed to establish its safety and efficacy, in the context of other mechanical approaches to GERD treatment that have shown benefits on the short-term but not on the long-term.

An ECRI clinical assessment on the LINX® Reflux Management System for treating GERD identified a review of evidence from 2017 through 2023, that included three systematic reviews, one randomized control trial, one patient registry study and two economic studies. The evidence appears to indicate that LINX may be safe and as effective as laparoscopic Nissen fundoplication, however the studies had a high risk of bias and not enough patients were included to confirm the conclusions. It was concluded larger multicenter RCTs and longer follow-up with comparisons of LINX with other GERD devices would be useful to determine long-term safety and efficacy (ECRI 2023).

A Hayes Health Technology Assessment (2022) evaluated the effectiveness and safety of magnetic sphincter augmentation (MSA) with the LINX Reflux Management System for the treatment of GERD. One RCT compared MSA with twice-daily PPI treatment and the other 5 nonrandomized cohort studies compared MSA with laparoscopic fundoplication (LF). While the low-quality body of evidence suggests that MSA may improve the patient's quality of life and their GERD symptoms along with a reduction in PPI use, there remains uncertainty about the long-term safety and efficacy of this device. The report overall conclusion is that there is potential but unproven benefit to the LINX system.

Zhuang et al. (2021, included in the Hayes report above) performed a systematic review and meta-analysis to determine the efficacy and safety of magnetic sphincter augmentation (MSA) in the management of refractory GERD as well as comparing MSA efficacy to proton pump inhibitor (PPI) or laparoscopic Nissen fundoplication (LNF). Ten single-arm studies, one randomized controlled trial and three cohort studies involving 1,138 participants were included. Post-MSA PPI withdrawal, significant GERD-HRQL improvement and AET normalization were achieved in 87.0%, 88.0% and 75.0% of the patients, individually. The incidence of postoperative dysphagia was 29% and endoscopic dilation was required in 7.4% of patients undergoing MSA. MSA showed a better efficacy in symptom control than PPI (PPI cessation: 91% vs. 0%; GERD-HRQL improvement: 81% vs. 8%) and similar effectiveness but a lower risk of gas-bloat syndrome [risk ratio (RR) 0.69, 95% confidence interval (CI) 0.51-0.93, p = 0.01] and better reserved ability to belch (RR 1.48, 95% CI 0.76-2.86, p = 0.25) compared with LNF. Study limitations included the following: limited number of clinical studies; only three studies were included in the comparative results between MSA and LNF; and potential for selection bias that could have led to an overestimation of efficacy in MSA since the patient selection had less severe GERD. The authors concluded that MSA was an effective and safe therapy for GERD for patients with PPI-refractory symptoms and pathological reflux. There was only one randomized comparative trial that presented an advantage over a double dose of PPI. Therefore, there is a need for additional randomized trials that compare the efficacy of MSA with other therapies. [Bonavina (2010), Lipham (2012), Ganz (2013 and 2016), Saino (2015) and Warren (2016) previously cited in this policy are included in this meta-analysis].

Chandan et al. (2021) conducted a systematic review and meta-analysis on patients undergoing treatment for refractory GERD and compared the efficacy of MSA with that of transoral incisionless fundoplication (TIF2). Twenty-four articles were included in the analysis which consisted of 1,074 patients that underwent MSA, and 868 patients underwent TIF2. In the MSA cohort, six studies were prospective, and 3 studies were retrospective; in the TIF cohort, eleven studies were prospective and four were retrospective. The authors found the clinical success rate, demonstrated by improvement of scores in GERD HRQL, was 80% for MSA and 77% for TIF. It was concluded that both procedures have a similar efficacy, but MSA seem to outperform TIF2. Overall, 91.3% of the MSA patients were able to discontinue PPI therapy compared to 63.8% of the TIF2 patients. Limitations included lack of long-term data.

Bell et al. (2020, included in Hayes report above) compared the effects of MSA versus PPI in a randomized trial. 152 patients with moderate to severe regurgitation symptoms across twenty-one U.S. clinical sites were randomized into two groups. Additional inclusion criteria for the participants were once daily PPIs for at least 8 weeks, body mass index < 35 kg/m^2, abnormal pH testing (DeMeester score < 4), hiatal hernia < 3 cm by endoscopy and absence of Barrett's esophagus or Los Angeles Classification Grade C or D esophagitis. Participants were assessed at 6 and 12 months with the Reflux Disease Questionnaire (RDQ) and the GERD Health Related Quality of Life (GERD-HRQL) standard assessments along with specific questions concerning bloating, diarrhea, flatulence, and medication use. One group (n = 102) received PPI (20 mg of omeprazole twice daily) and the other group (n = 50) received laparoscopic MSA. The authors found that MSA controlled regurgitation in 96% of patients versus only 19% of patients receiving PPIs reported control of regurgitation. The regurgitation had been sustained over 12 months. The second portion of the study allowed eligible patients (39%) from the PPI group to crossover and receive the laparoscopic MSA if they had not demonstrated improvement with the twice daily medication. The authors concluded MSA is an effective surgical treatment option for patients with medically refractory regurgitative GERD. The study is limited by limited follow-up.

Ferrari et al. (2020) followed a cohort of 124 individuals who underwent laparoscopic implantation of an MSA device. The goal was to assess the long-term safety and efficacy of the Linx Reflux Management System for 6-12 years. Prior to surgery, all patients completed a diagnostic assessment that included the GERD-HRQL questionnaire, upper GI endoscopy, barium swallow study, ambulatory esophageal pH monitoring and esophageal manometry. Success was defined as ≥ 50% improvement in the GERDHRQL total score and discontinuation of PPI medication. During follow up, over a five-year period, eight patients (2.4%) required a single endoscopic pneumatic dilation due to persistent dysphagia. Thirty-one patients (9.2%) required removal of the device for various reasons; erosion and regurgitation were the top two reasons with six patients each.

The average total GERD-HRQL score decreased from 19.9 (baseline) to 4.01. The authors found eighty-one percent of the patients had a successful clinical outcome and were able to discontinue their PPI use. Long-term results in thirty-two patients past 10 years found zero dysphagia, seven individuals with occasional PPI use and only 3 with daily PPI use. The

total overall patient satisfaction rate was 92.5%. The authors concluded MSA allows control of GERD symptoms and improvement in patient quality of life without significant safety issues. However, it was also concluded that additional RCTs could provide more definitive conclusions. Limitations included no comparison group and possible selection bias with large loss to follow up over time.

Schizas et al. (2020) conducted a systematic review to investigate the safety and efficacy of the LINX® Reflux Management System. After screening 614 articles, a total of 35 studies fit the criteria and were analyzed. According to the authors, although laparoscopic fundoplication (LF) and MSA both appear to be safe and effective procedures, MSA appears to have a few distinct advantages such as a less technical procedure, less bloating and superiority in the ability to vomit/belch, easily reversible and if it fails, LF is still a viable option after device removal. The authors' findings suggested that MSA with the LINX device is a safe procedure and has the potential to bridge the treatment gap between maxed out medical treatment and laparoscopic fundoplication. The authors also concluded that further studies with longer follow-up are needed. [Asti (2016), Desart (2015), Reynolds (2015), and Bonavina (2008 and 2010) previously cited in this policy are included in this systematic review.]

A prospective, multicenter, randomized control trial was conducted by Bell et al. (2019, included in the ECRI report) comparing magnetic sphincter augmentation (MSA) (n = 50) to double-dose proton-pump inhibitor (PPI) therapy (omeprazole, 20 mg, twice a day) (n = 102). The goal of the study was to compare the effect of the two treatments for elimination of moderate to severe regurgitation. As reported on a foregut symptom questionnaire, at six months, 89% of patients treated with MSA reported relief of regurgitation, with 81% reporting ≥ 50% improvement in GERD-health-related quality of life scores. Ten percent of the PPI group reported relief of regurgitation with eight percent of the PPI group reporting ≥ 50% improvement in GERD-health-related quality of life scores. However, twenty-eight percent of MSA patients reported transient dysphagia, with 4% reporting ongoing dysphagia. The authors concluded that patients who continue to experience moderate to severe regurgitation despite PPI treatment should be considered for MSA. Randomized controlled trials with larger patient populations and long term follow up are needed to further assess the long-term safety and efficacy of MSA.

Louie et al. [2018, included in the Schizas et al. (2020) systematic review above] reported one-year results from a mandated post-approval multicenter, prospective case series of 200 patients with pathologic acid reflux confirmed by esophageal pH testing, who underwent MSA. Predefined clinical outcomes were assessed at the annual visit including a validated, disease-specific questionnaire, esophagogastroduodenoscopy (EGD) and esophageal pH monitoring, and use of proton pump inhibitors. At 1 year, the mean total acid exposure time decreased from 10.0% at baseline to 3.6%, and 74.4% of patients had normal esophageal acid exposure time (% time pH < 4 ≤ 5.3%). GERD Health-Related Quality of Life scores improved from a median score of 26.0 at baseline to 4.0 at 1 year, with 84% of patients meeting the predefined success criteria of at least a 50% reduction in total GERD Health-Related Quality of Life score compared with baseline. The device removal rate at 1 year was 2.5%. There was a report of one erosion, and no serious adverse events were reported. Although the authors conclude that safety and effectiveness of MSA has been demonstrated outside of an investigational setting, study limitations include lack of contemporaneous comparison group receiving a different GERD treatment and relatively short follow-up period.

In a retrospective observational study, Warren et al. [2018, included in the Schizas et al. (2020) systematic review above] analyzed factors influencing the outcome of MSA for chronic GERD using data from a pivotal trial (n = 99) and the authors prospectively maintained esophageal database (n = 71). A priori outcomes were defined as excellent (GERD-HRQL < 5, no PPI, no esophagitis), good (GERD-HRQL 6-15, no PPI, grade A esophagitis), fair (GERD-HRQL 16 to 25, PPI use, grade B esophagitis), and poor (GERD-HRQL > 25, PPI use, grade C/D esophagitis). Univariable and multivariable logistic regression analyses were performed to determine predictors of achieving an excellent/good outcome. A total of 170 patients underwent MSA with a median age of 53 years, (43-60) and a median BMI of 27 (IQR = 24-30). At baseline, 93.5% of patients experienced typical symptoms and 69% atypical symptoms. At univariable analysis, excellent/good outcomes were negatively impacted by BMI, preoperative LES residual pressure, Hill grade, and hiatal hernia. At multivariable analysis, BMI > 35 (OR = 0.05, 0.003-0.78, p = 0.03), structurally defective LES (OR = 0.37, 0.13-0.99, p = 0.05), and preoperative LES residual pressure (OR = 0.89, 0.80-0.98, p = 0.02) were independent negative predictors of excellent/good outcome. The authors' conclusion is that MSA results in excellent/good outcomes in most patients but a higher BMI, structurally defective sphincter, and elevated LES residual pressure may prevent this goal. The authors' conclusion is that a higher BMI, structurally defective sphincter, and elevated LES residual pressure may prevent optimal treatment with MSA. The findings however do not provide evidence for the safety and efficacy of MSA compared to other therapeutic approaches.

Aiolfi et al. [2018, included in the Schizas et al. (2020) systematic review above] conducted a systematic review and meta-analysis of early results of MSA versus fundoplication for the treatment of GERD. Seven observational cohort studies, published between 2014 and 2017, matched the inclusion criteria. Overall, 1,211 patients, 686 MSA and 525 LF, were

included. Postoperative morbidity ranged from 0 to 3% in the MSA group and from 0 to 7% in the LF group, and there was no mortality. Dysphagia requiring endoscopic dilatation occurred in 9.3% and 6.6% of patients respectively (OR = 1.56, 95% CI = 0.61-3.95, p = 0.119). The pooled OR of gas/bloat symptoms, ability to vomit, and ability to belch were 0.39 (95% CI 0.25-0.61; p < 0.001), 10.10 (95% CI 5.33-19.15; p < 0.001), and 5.53 (95% CI 3.73-8.19; p < 0.001), respectively. The postoperative GERD-HRQL was similar (p = 0.101). The pooled OR of PPI suspension, endoscopic dilation, and reoperation were similar in the two patients' groups (p = 0.548, p = 0.119, p = 0.183, respectively). The authors concluded that both anti-reflux procedures are safe and effective up to 1-year follow-up. PPI suspension rate, dysphagia requiring endoscopic dilatation, and disease-related quality of life are similar in the two patient groups. MSA is associated with less gas/bloat symptoms and increased ability to vomit and belch. The findings are limited by inclusion of observational studies only and relatively short follow-up periods.

Alicuben et al. [2018, included in the Schizas et al. (2020) systematic review above] reported on the worldwide experience with erosion of the MSA device in a large case series. In total, 9,453 devices were placed and there were 29 reported cases of erosions. The median time to presentation of an erosion was 26 months with most occurring between 1 and 4 years after placement. The risk of erosion was 0.3% at 4 years after device implantation. Most patients experienced new-onset dysphagia prompting evaluation. Devices were successfully removed in all patients most commonly via an endoscopic removal of the eroded portion followed by a delayed laparoscopic removal of the remaining beads. At a median follow-up of 58 days post-removal, there were no complications and 24 patients have returned to baseline. Four patients reported ongoing mild dysphagia. The authors concluded that erosion of the LINX device is an important but rare complication to recognize that has been managed via minimally invasive approaches without long-term consequences. Continued monitoring and reporting of MSA erosion will provide longer-term experience.

In a systematic review and meta-analysis of the LINX® magnetic esophageal sphincter augmentation versus Nissen fundoplication for gastroesophageal reflux disease, Skubleny et al. (2017) included randomized controlled trials, non-randomized comparison study and case series with greater than 5 patients. Five hundred and forty-seven titles were identified through primary search, and 197 titles or abstracts were screened after removing duplicates. Meta-analysis was performed on postoperative quality of life outcomes, procedural efficacy, and patient procedural satisfaction. Three primary studies identified a total of 688 patients, of whom 273 and 415 underwent Nissen fundoplication and MSA, respectively. MSA was statistically superior to LNF in preserving patient's ability to belch (95.2 vs. 65.9%, p < 0.00001) and ability to emesis (93.5 vs. 49.5%, p < 0.0001). There was no statistically significant difference between MSA and LNF in gas/bloating (26.7 vs. 53.4%, p = 0.06), postoperative dysphagia (33.9 vs. 47.1%, p = 0.43) and PPI elimination (81.4 vs. 81.5%, p = 0.68). The authors' conclusion is that magnetic sphincter augmentation appears to be an effective treatment for GERD with short-term outcomes comparable to the more technically challenging and time-consuming Nissen fundoplication. The authors also concluded that long-term comparative outcome data past 1 year is needed in order to further understand the efficacy of magnetic sphincter augmentation.

Smith et al. (2017) reported that out of a total of 3,283 procedures reviewed for MSAD, device removal occurred in 2.7% of cases. The most common causes of removal were dysphagia, continued reflux, and device erosion into the esophagus. Salvador et al. (2017), Parmar et al. (2017), and Lipham, et al. (2015), report similar findings.

Ganz et al. [2016, included in the Schizas et al. (2020) and Zhuang et al. (2021) systematic reviews above] reported in a case series the 5-year follow-up evaluation of patients who received a magnetic sphincter augmentation (MSA) device for GERD. The original prospective study at 14 centers in the United States and the Netherlands was conducted on 100 adults with GERD for 6 months or more, who were partially responsive to daily proton pump inhibitors (PPIs) and had evidence of pathologic esophageal acid exposure. At baseline, the median GERD-HRQL scores were 27 in patients not taking PPIs and 11 in patients on PPIs; 5 years after device placement this score decreased to 4. All patients used PPIs at baseline; this value decreased to 15.3% at 5 years. Moderate or severe regurgitation occurred in 57% of subjects at baseline, but only 1.2% at 5 years. All patients reported the ability to belch and vomit if needed. Bothersome dysphagia was present in 5% at baseline and in 6% at 5 years. Bothersome gas-bloat was present in 52% at baseline and decreased to 8.3% at 5 years. The authors concluded that MSA provides significant and sustained control of reflux, with minimal side effects or complications, which in their opinion validates the long-term safety and efficacy of MSA for patients with GERD. The study is, however, limited by lack of comparison group.

Riegler et al. (2015, included in the Hayes report) evaluated using a retrospective cohort study design the evidence for magnetic sphincter augmentation device (MSAD) and laparoscopic fundoplication (LF) in clinical practice. Two hundred forty-nine patients (202 MSAD patients and 47 LF patients) had completed one-year follow-up. The LF group was older and had a greater frequency of large hiatal hernias and Barrett's esophagus than the MSAD group (p < 0.001). The median GERD-health related quality of life score improved from 20.0 to 3.0 after MSAD and 23.0 to 3.5 after LF. Moderate or severe regurgitation improved from 58.2 to 3.1% after MSAD and 60.0 to 13.0% after LF (p = 0.014). Discontinuation of PPIs was achieved by 81.8% of patients after MSAD and 63.0% after LF (p = 0.009). Excessive gas and abdominal

bloating were reported by 10.0% of patients after MSAD and 31.9% following LF ($p \leq 0.001$). Following MSAD, 91.3% of patients were able to vomit if needed, compared with 44.4% of those undergoing LF ($p < 0.001$). Reoperation rate was 4.0% following MSAD and 6.4% following LF. The authors conveyed that antireflux surgery should be individualized to the characteristics of each patient, taking into consideration anatomy and propensity and tolerance of side effects. They concluded that both MSAD and LF showed significant improvements in reflux control, with similar safety and reoperation rates. In their opinion, in the treatment continuum of antireflux surgery, MSAD should be considered as a first-line surgical option in appropriately selected patients without Barrett's esophagus or a large hiatal hernia in order to avoid unnecessary dissection and preserve the patient's native gastric anatomy. The study is, however, limited by lack of randomization.

Lipham et al. (2015) conducted a case series of antireflux surgery with a Magnetic Sphincter Augmentation Device (MSAD). The aim of the study was to examine the safety profile of the MSAD in the first 1,000 implanted patients. The author compiled data from multiple sources starting on July 1, 2013. The analysis included intra/perioperative complications, hospital readmissions, procedure-related interventions, reoperations, and device malfunctions leading to injury or inability to complete the procedure. The authors report that approximately 1,000 patients worldwide have been implanted with the MSAD, at 82 institutions with median implant duration of 274 days. They concluded that the safety analysis of the first 1,000 patients treated with MSAD for gastroesophageal reflux disease confirms the safety of this device and the implantation technique. The preliminary and positive results of this study are hampered by lack of an adequate comparator group.

Functional Lumen Imaging Probe (FLIP)

While the FLIP technology is used to enhance current procedures such as endoscopy, the evidence is insufficient for use in assessing esophageal and gastric disorders; additional research involving larger, RCTs with long-term outcomes is needed to establish its safety and efficacy.

Rafeeqi et al. (2023) analyzed the utility of EndoFLIP in diagnosis and management of achalasia in pediatric patients. The authors theorized that the distensibility index (DI) may aid diagnosis and treatment of pediatric achalasia. Thirty-three (21 male, 12 female) patients underwent POEM and EndoFLIP. The authors were able to show that certain measurements, such as Eckardt scores, had a direct correlation to achalasia symptoms. The higher the Eckardt score, the lower DI. While manometry is the current gold standard test for the diagnosis of achalasia, it is not tolerated well in children which makes the EndoFLIP a potential alternative for the pediatric population. The authors concluded that EndoFLIP could be beneficial in the pediatric population in the diagnosis and management of achalasia. The DI could be used to guide the extent of myotomy and monitor the results of any lower esophageal sphincter LES focused interventions, however, further studies are necessary to better support the use of EndoFLIP as a diagnostic tool. Limitations included small sample size, lack of manometry data for comparison and lack of long-term data.

A Hayes report (2022) for the use of EndoFLIP evaluated the device for its use in assessment of esophageal and gastric disorders. The evidence is insufficient to support any conclusions for any particular use of the device for any one disorder and found no improvement or benefit to health outcomes. Out of 13 studies, 11 reviewed and evaluated EndoFLIP for detecting or predicting disease course or treatment response. The other two studies evaluated the clinical utility for guidance and management of gastric disorders in addition to bariatric surgery. While the body of evidence for EndoFLIP was large for a variety of topics, the quality of evidence was low with a large range of uses. Limitations included lack of comparison groups, lack of systematic evaluation and lack of long-term outcomes.

An ECRI (2020) report on EndoFLIP for identification of GI motility disorders assessed two prospective and two retrospective single-center case series texts from January of 2015 thru May of 2020. The evidence found was considered inconclusive with mixed results. Limitations included a high risk of bias due to retrospective design, small sample size and lack of comparison groups.

In a systematic review, Desprez et al. (2020) summarized the available data in the literature on the use of the EndoFLIP® system in the gastrointestinal tract. A search was conducted using MEDLINE-PubMed, Cochrane Library, and Google Scholar databases. A total of 95 studies were found and 32 of these reported results in patients with achalasia. The authors found the EndoFLIP system demonstrated its relevance in the diagnosis of atypical achalasia and in the prediction of the treatment outcome in achalasia, but the precise esophago-gastric junction (EGJ) distensibility index (DI) threshold associated with success and prolonged response remains to be determined and therefore warrants additional studies. In addition, review of thirteen studies was completed which investigated EGJ in GERD patients. Patients were assessed with upper GI endoscopy and esophageal pH monitoring in addition to symptomatic evaluation. The authors found the patients with GERD seemed to have a higher EGJ DI than the healthy volunteers tested, but the relevance of the EndoFLIP system in the prediction of the efficacy of fundoplication remained unconfirmed. Limitations included no standard protocol found when using the EndoFLIP® in the esophagus along with cost and availability in daily practice. In conclusion, while the authors found EndoFLIP® might have some promise, its use in the body of the esophagus, other

esophageal diseases (GERD, eosinophilic esophagitis), and other sphincter regions (anal canal, pylorus) necessitates the need for additional confirmatory studies.

Yoo et al. (2019) assessed the utility of EndoFLIP in fifty-two patients with achalasia treated with POEM and hypothesized that improvement in the distensibility index (DI) correlated with the postoperative clinical outcome of POEM. EndoFLIP was performed before and after POEM by well-trained endoscopists in an outpatient setting. Esophagogastroduodenoscopy (EGD) was done just before EndoFLIP to measure esophageal length, four days following the procedure and again in outpatient clinic to evaluate the development of reflux esophagitis. The DI of the esophagogastric junction (EGJ) was measured at the point of narrowest perimeter of the functional lumen image during volumetric distension of the saline bag. After the probe was inserted, the DI and cross-sectional area (CSA) of the EGJ were measured at the site of the narrowest point. DI and CSA were measured twice during volumetric distension of the saline bag, each of them with 30 ml and 40 ml. The authors' conclusion was EndoFLIP was useful in predicting the treatment response and post-procedure reflux of POEM in patients with achalasia. Limitations included lack of comparison groups, lack of long-term outcomes and small sample size.

Clinical Practice Guidelines

American Gastroenterological Association (AGA)

The AGA recommends POEM be considered as a primary therapy for type III achalasia. Given the complexity of the POEM procedure, the AGA also recommends the procedure be performed by experienced physicians in high-volume centers to achieve procedure competence (Kahrilas et al., 2017).

An AGA clinical practice update (Khashab et al., 2023) on gastric peroral endoscopic myotomy for gastroparesis offered expert advice regarding cognitive, procedural, and post-procedural aspects on performance of gastric peroral endoscopic myotomy for the treatment of refractory gastroparesis. After review of the available evidence, it was concluded G-POEM is safe with a high technical success rate when performed by an experienced endoscopic specialist.

American Society for Gastrointestinal Endoscopy (ASGE)

In a 2015 clinical guideline on the role of endoscopy in the management of GERD, ASGE suggests that endoscopic antireflux therapy be considered for selected patients with uncomplicated GERD after careful discussion with the patient regarding potential adverse effects, benefits, and other available therapeutic options.

The ASGE identifies laparoscopic Heller myotomy, pneumatic dilation, and POEM as effective therapeutic modalities for patients with achalasia. The decision made between these treatment options should depend on achalasia type, local expertise, and patient preference (Khashab et al., 2020).

American College of Gastroenterology (ACG)

In a ACG clinical guideline (Camilleri, et al. 2022) for gastroparesis, the ACG suggests pyloromyotomy over no treatment for patients with gastroparesis that have not responded to medical therapy and continue to experience symptoms (conditional recommendation, low quality of evidence). The preferred myotomy method (laparoscopic or endoscopic) is however, not specified.

In a 2021 ACG published clinical guideline (Katz, et al. 2021) for the diagnosis and management of GERD, the following recommendations are cited:

- Recommend antireflux surgery as an option for long-term treatment of patients with objective evidence of GERD, (strong recommendation; moderate level of evidence).
- Recommend consideration of magnetic sphincter augmentation (MSA) as an alternative to laparoscopic fundoplication for patients with regurgitation who fail medical management (strong recommendation, moderate level of evidence).
- Consideration of transoral incisionless fundoplication (TIF) for patients with troublesome regurgitation or heartburn who do not wish to undergo antireflux surgery and who do not have severe reflux esophagitis or hiatal hernias (conditional recommendation; low level of evidence).
- Do not recommend radiofrequency energy (Stretta) as an antireflux procedure due to inconsistent data on the efficacy of the device (conditional recommendation; low level of evidence).

American Society of General Surgeons (ASGS)

In 2014, the ASGS published a position statement regarding its support for the LINX procedure. ASGS states that total management of GERD will likely rely upon a combination of medical and surgical care in the current and near future. ASGS recommends that when considering a surgical procedure, the procedure will need to provide safe control of GERD with minimal side effects. The ASGS states, "Based on currently available information and the experience of our members

with the procedure, we do support the LINX procedure as a mechanism for controlling GERD when it is placed by properly trained laparoscopic surgeons with experience in foregut surgery and the management of GERD patients."

In April 2011, the ASGS published a position statement regarding the use of TIF stating that it supports the use of TIF in patients with symptomatic chronic GERD who are not responsive to a standard dose of PPI therapy (ASGS, 2011). The ASGS also supports its use for patients who wish to avoid lifetime drug therapy for this condition. The ASGS also supports the adoption of the procedure by trained general surgeons as a less invasive alternative to more conventional surgical techniques, stating that the preferred surgical technique should be based on the discretion and judgment of the surgeon and the patient's clinical circumstances.

In a statement regarding coverage for TIF, ASGS states that there is a sufficient body of peer reviewed literature that establishes transoral fundoplication as reasonable and medically necessary for a subset of patients who are candidates for surgical fundoplication; specifically, patients who either cannot obtain satisfactory relief from standard PPI therapy or who wish to avoid a lifetime of dependence on such medications, and present with a 2 centimeter or smaller hiatal hernia (ASGS, 2011).

National Institute for Health and Care Excellence (NICE)

The National Institute for Health and Care Excellence (NICE, 2023) conducted a rapid review of the published literature on the efficacy and safety of laparoscopic insertion of a magnetic ring for gastro-esophageal reflux disease (GORD). They evaluated evidence from three systematic and meta-analyses, one RCT, three non-randomized comparative studies, and two case series. The committee noted that the magnetic ring use has evolved over time and is considered adequate. In addition, it was stated that the use of the device should be performed by clinicians that have specific training in the procedure.

The NICE guideline on endoscopic radiofrequency ablation for GERD considers the evidence on this procedure to be adequate in the short and medium term but there is uncertainty about longer-term outcomes. Regarding efficacy, there is evidence of symptomatic relief but objective evidence on reduction of reflux is inconclusive (NICE, 2013).

Society of American Gastrointestinal and Endoscopic Surgeons (SAGES)

SAGES guidelines (Kohn et al., 2021) on the use of POEM for the treatment of achalasia make the following recommendations:

- The panel suggests that adult and pediatric patients with type I and II achalasia may be treated with either POEM or laparoscopic Heller myotomy based on surgeon and patient's shared decision-making (conditional recommendation, very low certainty evidence).
- Based on the panel's collective experience, they suggest POEM over laparoscopic Heller myotomy for type III adult or pediatric achalasia (expert opinion).

The following recommendations are made by SAGES (Auyang et al., 2013) on endoluminal treatments for GERD:

- Results for EsophyX appear to be mixed and lacking long term data. Further studies are required to define optimal techniques and to further evaluate the device and its safety (Quality of Evidence: (++). GRADE Recommendation: Weak).
- The evidence for the Stretta device demonstrates it is considered appropriate therapy for patients > than 18 years of age with GERD and show symptoms of heartburn, regurgitation, or both for 6 months or more, have been partially or completely responsive to anti-secretory pharmacologic therapy, and have declined laparoscopic fundoplication (Quality of Evidence: (++++). GRADE Recommendation: Strong).

The SAGES Technology and Value Assessment Committee (TVAC) updated its safety and effectiveness analysis of the LINX Reflux Management System.

- Review of published studies suggests that magnetic sphincter augmentation is safe with no reported deaths and a 0.1% rate of intra/perioperative complications.
- Long-term efficacy of LINX appears good for typical GERD symptoms with reduced acid exposure, improved GERD symptoms, and freedom from PPI in 85-88% at 3-5 years.
- Dysphagia resolves in most patients and the incidence is roughly 10% at 1 year and 4% at 3 years. The need for endoscopic dilation ranges from 6-12% and the primary reason for explanation appears to be persistent dysphagia with a rate in larger series from 3-6%.
- Erosion appears to be rare, with one case reported in the 1st 1,000 patients, one additional published case report, a large series reporting 2 erosions, and several additional reports in the FDA MAUDE dataset (true number unknown, as multiple entries in this dataset may be made for each patient). Based on very limited literature, erosion can be successfully treated with explanation (Telem et al., 2017).

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Several endoscopic antireflux (endoluminal) devices have received approval by the FDA for treatment of gastroesophageal reflux disease (GERD).

The Stretta System (Mederi Therapeutics) was approved in April 2000, for radiofrequency thermal ablation treatment of GERD. Additional information is available at: http://www.accessdata.fda.gov/cdrh_docs/pdf10/k103017.pdf. (Accessed July 14, 2023)

The Bard EndoCinch Endoscopic Suturing System (Bard Endoscopic Technologies, Billerica, MA, a subsidiary of C.R. Bard Inc), was approved in January 2001, for endoscopic suturing in the treatment of GERD. Subsequent FDA approval was received in September 2007, for an updated version. Additional information is available at: http://www.accessdata.fda.gov/cdrh_docs/pdf7/k071651.pdf. (Accessed July 14, 2023)

The NDO Surgical Endoscopic Plication System was approved in September 2007, for endoscopic suturing in the treatment of GERD in patients who require and respond to pharmacological therapy. Additional information is available at: http://www.accessdata.fda.gov/cdrh_docs/pdf7/k071651.pdf. (Accessed July 14, 2023)

The current generation of EsophyX, EsophyX2, was cleared for marketing as substantially equivalent to the original EsophyX system with minor changes in November 2009 under the FDA510(k) process. The original system was cleared for marketing in September 2007, as substantially equivalent to the predicate devices NDO Surgical Endoscopic Plication System, Bard EndoCinch, and EGS StomaphyX Endoluminal Fasteners and Delivery System. According to the approval summary letter, EsophyX2 is indicated for:

- Use in transoral tissue approximation.
- Full-thickness plication and ligation in the GI tract.
- The treatment of symptomatic chronic gastroesophageal reflux disease in patients who require and respond to pharmacologic therapy.
- Narrowing of the gastroesophageal junction.
- Reduction of hiatal hernia < 2 cm in patients with symptomatic chronic gastroesophageal reflux disease.

Refer to the following websites for more information:

- http://www.accessdata.fda.gov/cdrh_docs/pdf7/K071651.pdf
- http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm?db=PMN&id=k092400

(Accessed July 14, 2023)

The Medigus Ultrasound Surgical Endostapler (MUSE™ System) received 510K approval on January 15, 2015, for the endoscopic placement of surgical staples in the soft tissue of the esophagus and stomach in order to create anterior partial fundoplication for treatment of symptomatic chronic GERD in patients who require and respond to pharmacological therapy. Refer to the following website for additional information: https://www.accessdata.fda.gov/cdrh_docs/pdf14/k143634.pdf. (Accessed July 14, 2023)

The EndoFLIP® System is indicated for use in a clinical setting to measure pressure and dimensions in the esophagus, pylorus, and anal sphincters and received 510K approval on April 17, 2017. It is intended to be used as an adjunct procedure to other diagnostic methods as part of a comprehensive evaluation of patients with symptoms consistent with gastrointestinal motility disorders. Refer to the following website for additional information: https://www.accessdata.fda.gov/cdrh_docs/pdf17/K170833.pdf. (Accessed July 14, 2023)

These products are Class II devices (moderate risk) deemed substantially equivalent to other endoscopic devices utilizing other procedures.

Torax Medical obtained FDA premarket approval (PMA) in March 2012, for the LINX Reflux Management System. Additional approvals for PMA supplements can be found on the FDA website. Refer to the following website for more information using PMA number P100049: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm. (Accessed July 14, 2023)

Durasphere is approved by the U.S. Food and Drug Administration (FDA) as an injectable bulking agent for gastro-urology use in the treatment of adult women with stress urinary incontinence due to intrinsic sphincter deficiency. Use of this

product for esophageal reflux would be considered off-label use. Refer to the following website for more information, using PMA number P980053: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm. (Accessed July 14, 2023)

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Policy History/Revision Information

Date	Summary of Changes
07/01/2024	• New Medical Policy

Instructions for Use

This Medical Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Policy is provided for informational purposes. It does not constitute medical advice.

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