Endoscopic Procedures for Gastroesophageal Reflux Disease (GERD)

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INSTRUCTIONS:

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**POLICY DESCRIPTION:**

This policy describes the use of endoscopic procedures for the treatment of Gastroesophageal Reflux Disease (GERD). These are minimally invasive procedures using an endoscope rather than external incisions to reach the affected area of the digestive tract.

Traditional treatments for GERD involve lifestyle and diet changes as the first line of treatment. If these changes don't work, medications can be used. Surgical options, open or laparoscopic fundoplication, are also available.

Endoscopic procedures for GERD are designed to alter structures at the gastroesophageal junction to prevent reflux of gastric contents. There are three types of procedure for endoscopic treatment of GERD.

1. **Suturing Methods.** These methods use stitches, or sutures, at the lower end of the esophagus in a procedure called endoluminal gastric plication. The Endocinch is like a little sewing machine.
2. **Radio Frequency Method.** This method uses heat from radio frequencies to alter the muscles in the lower esophagus. Stretta is approved by the FDA for this purpose.
3. **Injection Method.** For this method, inert chemical or biochemical compounds were injected into the tissue of the lower esophagus. Enteryx was the component of choice, but is no longer approved by the FDA.

Endoscopic treatments have only been available for a few years, so not much research is available on long-term effectiveness and safety of such procedures. Therefore, these procedures are considered investigational and/or experimental for the management of patients with GERD. Traditional surgeries for GERD still have a higher long-term success rate than the newer endoscopic treatments.

**COVERAGE RATIONALE / CLINICAL CONSIDERATIONS:**

- **Radiofrequency ablation,** as an alternative to esophagectomy, is considered **MEDICALLY NECESSARY** in individuals with:
  1. Barrett’s esophagus with high-grade dysplasia, confirmed by endoscopy, or
  2. Barrett’s esophagus with low-grade dysplasia (LGD), confirmed by a biopsy finding of LGD

  Endoscopic radiofrequency ablation is considered **INVESTIGATIONAL AND EXPERIMENTAL** and therefore **NOT MEDICALLY NECESSARY** for Barrett’s esophagus without dysplasia.

  **Note:** Local Coverage Determination for Endoscopic Treatment of GERD (L30473), CMS addresses that benefits are not available for radiofrequency energy delivered to the smooth muscle of the lower esophageal sphincter (LES) to treat GERD, as these procedures are not considered reasonable and necessary. See the Regulatory Status/CMS/LCD section.

- **Endoscopic implantation of Inert Polymers or polymethylmethacrylate (PMMA) beads (e.g., LINX Reflux Management System sphincter augmentation device),** is considered **MEDICALLY NECESSARY** for the treatment of severe or life threatening Gastro Esophageal Reflux Disease (GERD), in individuals whose conditions have been resistant to medical treatment, and who also present any of the following clinical situations:
  1. Have esophageal involvement with progressive systemic sclerosis, or
  2. Have foreshortening of the esophagus such that insufficient tissue exists to permit a valve
reconstruction, or
3. Are poor surgical candidates for a valvuloplasty procedure, or
4. Have failed previous attempts at surgical treatment with valvuloplasty procedures.

- The following transesophageal endoscopic therapies and procedures are considered EXPERIMENTAL AND/OR INVESTIGATIONAL for the management of patients with gastro-esophageal reflux disease (GERD) and all other indications:

1. Endoscopic gastroplasty/gastroplication suturing
   - Bard EndoCinch Suturing System (Bard Endoscopic Technologies)
   - Endoscopic Suturing Device® (Wilson-Cook Medical)
   - EsophyX or StomaphyX System, EsophyX2 System, SerosaFuse Fastener (transoral incisionless fundoplication procedure) (EndoGastric Solutions)
   - Endoscopic Plicator System (NDO Surgical, Inc.)
   - Syntheon ARD Plicator (Syntheon)

2. Radiofrequency energy delivery
   - Stretta® System (Curon Medical Inc.)

3. Implantation of Inert Polymers or polymethylmethacrylate (PMMA) beads
   - Durasphere (Carbon Medical Technologies)
   - Gatekeeper™ Reflux Repair System (Medtronic, Inc.)
   - The Plexiglas (polymethylmethacrylate microspheres [PMMA]) (Röhm GmbH & Co. KG, Darmstadt, Germany)
   - Enteryx® Procedure Kit (Boston Scientific Corporation)
   - LINX Reflux Management System sphincter augmentation device (Torax Medical).  
   **Note:** CMS has medical necessity benefits guidance for the LINX Reflux Management System.  
   See the Regulatory Status/CMS/LCD section, National Coverage Determination for endoscopic implantation of Anti-Gastroesophageal Reflux Device (100.9).

4. Angelchik anti-reflux prosthesis

The safety and efficacy of endoscopic therapies for the treatment of GERD have not been established in the published peer-reviewed medical literature. Well designed studies are needed to support the use of any minimally invasive transesophageal endoscopic procedures/therapies for GERD and to establish long-term improved patient health outcomes by eliminating symptoms, preventing recurrence of symptoms or progression of disease, healing esophagitis, and reducing the need for pharmacologic therapy.

**Clinical Considerations:**
Relative contraindications include:
- Atypical GERD symptoms,
- Other associated foregut pathology (specifically, gastroparesis)
- Psychoemotional disorders
- Functional esophageal disease
- Bleeding disorders
- Esophageal strictures/varices
- High-grade dysplasia or cancer
- Shortened esophagus
- Collagen vascular disease
- Peptic stricture
- Patients who are pregnant
- Poor surgical candidates
- Morbidly obese

**BACKGROUND:**

Gastroesophageal reflux disease (GERD) affects 10% to 20% of the world population. This chronic disorder is associated with a risk of significant morbidity, substantially impacting quality of life (QOL), and the possibility of mortality from complications. Approximately 44% of the American population experience gastroesophageal symptoms at least once a month, and up to 10% experience symptoms on a daily basis. The prevalence of GERD in the United States is estimated at 19 million cases per year, with an associated total cost of care of $9.8 billion. The single largest component of the cost of care of these patients is drug costs, estimated at $5.8 billion (Sandler et al., 2002; Dent et al., 2005).

GERD is due to recurring reflux, or regurgitation, of the stomach contents into the esophagus, which results in the classic symptoms of heartburn—a burning, acidic feeling in the throat and chest. In its mildest form, GERD is an annoyance necessitating control with lifestyle modification, antacids, or over-the-counter (OTC), acid-secretion suppressive medications. However, while reflux typically manifests itself as heartburn, regurgitation, or difficulty swallowing (dysphagia), it also can lead to complications such as esophagitis, an inflammatory condition caused by chronic irritation of the esophageal lining by stomach acids and enzymes; esophageal erosion, or ulceration; esophageal stricture; and Barrett’s esophagus, a premalignant condition to esophageal adenocarcinoma.

In patients with GERD, the lower esophageal sphincter (LES) maintains insufficient tension to prevent reflux from the stomach into the esophagus. Inappropriate transient relaxations of the LES (tLESRs), increasing the frequency and duration of esophageal reflux, are responsible for reflux events in patients with normal LES pressure. Other factors that may contribute to the development of GERD include hiatal hernia, esophageal motility disorders, decreased salivary clearance of reflux, decreased secretion of bicarbonate in the esophagus, increased susceptibility of the esophageal lining to damage by gastric secretions, and delayed gastric emptying. Besides the classic symptoms of heartburn and acid regurgitation, other atypical signs and symptoms of GERD, such as chest pain, hoarseness, nausea, chronic cough, pain on swallowing, dental enamel loss, and asthma, may be present.

Diagnosis of GERD accompanied by classic symptoms usually can be made on the basis of history, clinical presentation, and response to acid-suppressing medications. While there is no gold standard for diagnosing GERD, ambulatory 24-hour pH monitoring is the accepted standard for establishing or excluding its presence. In patients with nonerosive reflux disease or symptomatic reflux esophagitis, this test has a sensitivity and specificity of 70% to 96%. The test involves placement of a pH monitor in the esophagus above the LES, with measurements taken periodically. The patient keeps a journal, and the pH value, patient activity, and symptoms for each time point are correlated. Endoscopy is the gold standard for assessing esophageal complications of GERD, although this procedure lacks sensitivity for the diagnosis of GERD, itself. Esophageal manometry testing, which involves pressure measurements across the LES,
generally is used in severe cases or when a patient with reflux is being considered for surgery.

The primary treatment goals of GERD are relief of symptoms, prevention of symptom relapse, healing of erosive esophagitis, and prevention of GERD-related complications. In patients with reflux esophagitis, treatment is directed at acid suppression through the use of lifestyle modifications and pharmacologic agents. Lifestyle modifications include elevating the head of the bed, modifying the size and composition of meals, weight loss, smoking cessation, and avoiding a reclining position 3 hours after eating. Pharmacologic agents include acid suppressants and antacids, histamine-2 receptor antagonists (H2RAs), or proton pump inhibitors (PPIs). Pharmaceutical agents can lose their effectiveness over time, requiring progressively higher dosing. Adults affected by GERD who no longer respond adequately to drugs or those who wish to discontinue use of these medications have the option of laparoscopic antireflux surgery, commonly referred to as laparoscopic Nissen fundoplication. While this surgery has long proven to be effective in treating the disease, the procedure is invasive and potential side effects of the fundoplication procedure may compromise otherwise excellent postsurgical results. A transoral incisionless fundoplication procedure was developed to mimic anti-reflux surgery, as a minimally invasive alternative procedure with potentially fewer side effects.

Endoscopic, or endoluminal, therapies for GERD are designed to alter structures at the gastroesophageal junction to prevent reflux of gastric contents. These therapies are to provide an option for patients who would prefer nonpharmacologic therapy but wish to avoid anti-reflux surgery. Current techniques are less invasive than antireflux surgery and are performed in the outpatient setting. They may be classified into three basic categories:

1. Endoscopic or plication suturing of the proximal stomach (Bard EndoCinch Suturing System)
2. Radiofrequency energy delivered to the gastroesophageal junction (Stretta System)
3. Polymer injection or implantation of bulking agents into the cardia or distal esophagus (EsophyX System with SerosaFuse Fastener)

**Bard EndoCinch Suturing System:**
This is the first approved endoscopic suturing procedure. It requires two endoscopes and an overtube, and involves placing sutures just below the gastroesophageal junction to create an internal plication of the stomach, “tightening” the cardiac component of the LES and imposing a barrier to reflux. Stitches are placed into adjoining proximal gastric folds (not into the muscular portion) to create pleats. The first endoscope carries the metal sewing capsule on its tip, and the second endoscope cinches the sutures using a catheter device that deploys a ceramic plug and ring through which the sutures are threaded. Target tissue is drawn into the sewing chamber via suction, and two sutures are placed into the tissue. An extracorporeally tied knot then is advanced through the endoscope to create a single plication, formed by the two sutures. A short overtube, which is reusable, allows for repeated intubations (approximately 10). Two to three plications usually are performed longitudinally, radially, or spirally at the side of the cardia with lesser curvature within 1 cm below the squamocolumnar junction. The EndoCinch device has both single use and reusable components. The procedure typically is performed on an outpatient basis using either conscious or deep sedation and takes approximately 60 minutes. The patient resumes normal activities the next day. Considerable endoscopic skill and expertise is needed to perform the procedure, and endoscopists are required to undergo manufacturer training at an animal facility (Falk et al., 2006b).

**Stretta System:**
The Stretta Procedure is endoscopically-guided and minimally invasive. Radiofrequency energy delivery requires a special single-use catheter and radiofrequency energy generator. The flexible delivery catheter is
made up of a soft shaft and a balloon-basket assembly with four electrodes positioned radially around the balloon. The generator delivers radiofrequency energy to the catheter in an automated fashion under temperature control using thermocouple monitoring, and the power output is regulated by computer algorithm. When the catheter is positioned and the needles deployed into the circular muscle of the gastroesophageal junction, energy is delivered to each electrode to create a series of thermal lesions in the muscle of the LES and gastric cardia. Target tissue and mucosal temperature are achieved and maintained through a special suction and irrigation system.

The Stretta procedure usually is performed on an outpatient basis in the endoscopy unit or ambulatory surgery center with the use of intravenous conscious sedation. Radiofrequency energy is delivered while the mucosa is cooled with irrigation, using the previously described temperature-controlled radiofrequency generator system. The procedure generally takes under 40 minutes, and the patient typically resumes normal activity the next day. Patients undergo endoscopy immediately after delivery of radiofrequency energy to assess the post radiofrequency appearance of the mucosa. Typically, collagen contraction is observed immediately after radiofrequency energy delivery with tightening of the gastroesophageal junction.

**EsophyX System with SerosaFuse Fastener:**

The EsophyX/SerosaFuse system consists of sterile polypropylene fastener implants and a flexible fastener delivery device. The SerosaFuse fasteners and EsophyX delivery device are provided sterile and are for single use. The polypropylene fasteners are proprietary and function only with the EGS delivery devices. The transoral incisionless fundoplication procedure using the EsophyX/SerosaFuse system creates full-thickness serosa-to-serosa plications and constructs valves 3 to 5 cm (centimeters) in length and 200° to 300° in circumference. The procedure is performed with the patient under general anesthesia, typically by a team of physicians. One physician controls the implantation of fasteners using the EsophyX device, and the other ensures continuous direct visualization with an endoscope. The surgery generally takes less than an hour, and most patients go home the next day. Patients are instructed to consume a liquid diet during the first 2 weeks and a soft diet during the following 4 weeks. In general, proton pump inhibitors are discontinued 7 days after the procedure. The EsophyX/SerosaFuse system is indicated for the treatment of symptomatic chronic GERD in patients who require and respond to pharmacological therapy. It is also indicated to narrow the gastroesophageal junction and reduce hiatal hernia < 2 cm in size in patients with symptomatic chronic GERD.

**Transesophageal Endoscopic Injection and Implantation techniques:** Endoscopic injection and implantation techniques involve endoscopic injection or implantation of inert polymer material into the submucosa of the proximal lower esophageal sphincter (LES) zone to provide bulking support to the sphincter to help prevent acid reflux. Usually performed in an endoscopy suite or ambulatory surgery center using intravenous conscious sedation, these procedures are intended for patients with symptomatic GERD.

There are three endoscopic injection and implantation techniques (also referred to as bulking techniques) currently under investigation:

- The Plexiglas (polymethylmethacrylate [PMMA]) procedure which involves injection of an inert polymer material into the submucosa of the proximal lower esophageal sphincter zone to provide bulking support to the sphincter and decrease transient relaxations of the lower esophageal sphincter (tLESRs).
- The Gatekeeper Reflux Repair System utilizes a soft, pliable, expandable prosthesis made of a
polyacrylonitrile-based hydrogel. The prosthesis is implanted into the esophageal submucosa, and with time, the prosthesis absorbs water and expands, creating bulk in the region of implantation. These agents are not commercially available in the United States.

- The bulking agent, pyrolytic carbon-coated beads (Durasphere®), is being evaluated for treatment of GERD. Durasphere is approved by the U.S. Food and Drug Administration (FDA) as a submucosal urethral bulking agent. Use of this product for esophageal reflux would be considered off-label use

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 Web site, the LINX system is a small flexible band of interlinked titanium beads with magnetic cores. The magnetic attraction is intended to help the lower esophageal sphincter (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.

**Radiofrequency ablation (RFA), using the HALO system (BÄRRX Medical Inc., Sunnyvale, CA):** Barrett’s esophagus (BE) is a condition in which the normal squamous epithelium of the esophagus is replaced by an abnormal, specialized columnar type epithelium, similar to the lining of the intestine. This process is called intestinal metaplasia. Intestinal metaplasia is a precursor to esophageal adenocarcinoma and persons with BE are at a 40-fold increased risk for developing this disease compared to the general population. Management of Barrett’s esophagus (BE) is dependent on the progression of the disease and may include treatment of GERD, surveillance, and a number of endoscopic or surgical procedures. Radiofrequency ablation (RFA), using the HALO system (BÄRRX Medical Inc., Sunnyvale, CA), is under investigation as a non-invasive therapy for BE. RFA consists of a sizing balloon, an energy generator, and an ablation catheter, which deliver radiofrequency energy under endoscopic guidance, purportedly removing the diseased tissue lining the esophagus.

**REGULATORY STATUS:**

1. **U.S. FOOD AND DRUG ADMINISTRATION (FDA):**

   Several endoscopic antireflux (endoluminal) procedures have received approval by the U.S. Food and Drug Administration (FDA) for treatment of gastroesophageal reflux disease (GERD).


EsophyX, EsophyX2: 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 U.S. Food and Drug Administration's (FDA) 510(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, and
- Reduction of hiatal hernia <2 cm in patients with symptomatic chronic gastroesophageal reflux disease.


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

Enteryx™: The Enteryx™, a biocompatible liquid polymer, received FDA approval in 2003 through the premarket approval (PMA) process for the treatment of symptomatic GERD. However, on September 22, 2005, Boston Scientific Corporation issued a recall of Enteryx due to the device polymerizing shortly after injection into a spongy material that cannot be removed. Serious adverse events involved unrecognized transmural injections of Enteryx into structures surrounding the esophagus, potentially resulting in serious injury or death. See the following Web site for more information:

HALO system (BÂRRX Medical Inc., Sunnyvale, CA): In June 2005, the U.S. Food and Drug Administration (FDA) granted 510(k) clearance for the HALO360 Coagulation System for use in the coagulation of bleeding and nonbleeding sites in the gastrointestinal tract, including the treatment of Barrett’s esophagus (BE). The HALO90 System received FDA approval in April 2006. The HALOFLEX Energy Generator received 510(k) approval in November 2009.

2. CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS):

National Coverage Determination (NCD):

National Coverage Determination for endoscopic implantation of Anti-Gastroesophageal Reflux Device (100.9): The procedure involves the implantation of this special device around the esophagus under the diaphragm and above the stomach, which is secured in place by a circumferential tie strap. The implantation of this device may be considered reasonable and necessary in specific clinical situations where a conventional valvuloplasty procedure is contraindicated. The implantation of an anti-gastroesophageal reflux device is covered only for patients with documented severe or life threatening gastroesophageal reflux disease whose conditions have been resistant to medical
treatment and who also:

1. Have esophageal involvement with progressive systemic sclerosis, or
2. Have foreshortening of the esophagus such that insufficient tissue exists to permit a valve reconstruction, or
3. Are poor surgical candidates for a valvuloplasty procedure, or
4. Have failed previous attempts at surgical treatment with valvuloplasty procedures.

**Note:** Endoscopic implantation of Inert Polymers or polymethylmethacrylate (PMMA) beads (e.g., LINX Reflux Management System sphincter augmentation device) is a good example.


**Local Coverage Determinations (LCD):**

LCDs addressing endoscopic treatments for GERD exist and compliance with these policies is required where applicable.

Local Coverage Determination (LCD): Category III CPT® Codes (L33392) states CPT code 0392T (laparoscopy, surgical, esophageal sphincter augmentation procedure, placement of sphincter augmentation device (i.e., magnetic band) as of 10/01/2015 is considered not medically necessary.


**3. MINNESOTA DEPARTMENT OF HUMAN SERVICES (DHS):**

Minnesota DHS does not have a policy statement regarding endoscopic procedures for the treatment of GERD in its Provider Manual or other specific provider references.

MHCP will cover fundoplication surgeries for the long-term management of adults with chronic GERD as medically necessary. In order for the authorization request to be approved, patients must meet all of the following authorization criteria:

- GERD symptoms are refractory to ongoing medical management for a period of at least six months, which must include both of the following:
  - Treatment with proton pump inhibitors (PPIs)/histamine type 2 receptor antagonists (H2RAs) with appropriate titration of dosing.
  - Non-pharmacologic management, including lifestyle and behavioral modifications, including dietary changes, body positioning, antacid use, and tobacco cessation if applicable.
  - REQUIRED DOCUMENTATION: Written description of medical management and patient’s response.

- Patient has undergone a positive endoscopic evaluation (showing moderate or severe erosion, ulcerations, strictures, or Barrett’s esophagus) after a minimum of 8 weeks of medical management without sufficient symptom relief.

  REQUIRED DOCUMENTATION: Date of endoscopy and written description of findings.
## CLINICAL EVIDENCE:

### SUMMARY:

**Bard EndoCinch Suturing System:**

Results of the first prospective multicenter trial on the endoscopic plication suturing technique, EndoCinch, suggested that the procedure was safe and associated with improved symptom control and reduction in the use of medications at the 6-month follow-up in patients with early-stage uncomplicated GERD. QOL results showed a significant improvement in bodily pain, and there was a reduction in esophageal acid reflux. However, there was no difference in LES pressure measurements (Filipi et al., 2001). Small study size, short follow-up, and lack of a comparison group, as well as a 20% dropout rate and 17% retreatment rate, were limitations of this early study on EndoCinch.

Two small, uncontrolled prospective studies evaluated the efficacy of endoluminal plication suturing after 12 months. The first study reported that endoscopic suturing was a safe procedure, resulting in modest alterations in LES function. These changes were associated with minor, but significant, improvements in reflux control that were sustained at 12 months, including improvement in QOL and reduction in severity of reflux symptoms. However, after 6 months, plication loss was shown in 40% of the patients (Tam et al., 2004). In the second study, beneficial effects of the suturing treatment were reported on GERD symptoms, PPI use, and esophageal acid exposure. However, after 12 months, none of the patients still had correct placement of all of the initial sutures. This was considered a serious failure of the technique (Abou-Rebyeh et al., 2005). Limitations of both studies included size and lack of a control group.

There were two moderate-size, uncontrolled prospective studies with longer follow-up (18 and 24 months) that evaluated the efficacy of EndoCinch. At 18 months follow-up, Schiefke et al. (2005a) reported an improvement in heartburn severity symptoms but not in medication use, esophageal acid exposure, or LES pressure. In addition, the study reported mild and transient adverse events, with a high degree of suture loss (83%). Chen et al. (2005) reported significant reductions in medication use and GERD symptoms at 24 months follow-up. These results suggest a decrease in esophageal acid exposure, but this outcome was only measured after 6 months follow-up. The authors estimated the annual antisecretory medication costs before and after treatment. An 88% reduction of the annual GERD-related costs was reported (from $1564 to $183 at 24 months). Adverse events were reported with care, but none were considered serious adverse events. The study was limited by the inclusion of moderate to severe GERD patients, lack of control group, and lack of follow-up assessment of the suture integrity (Chen et al., 2005).

One prospective, randomized study compared the endoluminal plication suturing technique, EndoCinch, with the polymer injection technique, Enteryx (Domagk et al., 2006). The two endoscopic techniques seemed equally successful in the treatment of GERD in terms of safety, reducing PPI usage and improving symptoms (heartburn symptoms score, modified DeMeester score, gastrointestinal life quality index, and SF-36). Esophageal acid reflux did not decrease significantly in either of the two groups, and a loss of 19% of suture material was reported in the EndoCinch group. A disadvantage of the study was that retreatment was allowed, which may have overstated the short-term efficacy of the treatments. In addition, study follow-up was short (6 months), study size was small (n=49), and the study lacked a control group. Two randomized, sham-controlled trials were performed to evaluate the safety and efficacy of EndoCinch (Montgomery et al., 2006; Schwartz et al., 2007). The first study demonstrated no complications and a positive short-term (3 months) effect on reflux symptoms and PPI use, which was lost at 12 months. No treatment effect was shown on esophageal acid exposure, and a 37% suture loss was reported.
(Montgomery et al., 2006). The second study included an observation group to measure the placebo effect of the sham procedure. EndoCinch was found to be safe (no adverse events), and it improved PPI use, GERD symptoms, and QOL scores compared with the sham procedure. However, there was no increased improvement in esophageal acid exposure in the EndoCinch group compared with the sham group, and a large percentage (81%) of loose sutures were observed during retreatment of nonresponders (Schwartz et al., 2007). The limitations of both studies included small size (n=46 and 60 respectively) and short follow-up.

Overall, the evidence from these studies suggests that EndoCinch may improve GERD symptoms and QOL scores, at least in the short term, and may reduce medication use in some patients. However, in the majority of studies, esophageal acid exposure and LES pressure were not improved, and rates of suture loss were high.

**Stretta System:**

Triadafilopoulos et al. (2001) conducted two prospective, multicenter trials in patients with a heterogeneous spectrum of clinical disease severity, but with minimal active esophagitis or hiatal hernia. The first study followed 47 patients for 6 months (Triadafilopoulos et al., 2001), and the second followed 118 patients for 12 months (Triadafilopoulos et al., 2002). Both studies reported that radiofrequency energy delivery significantly improved GERD symptoms, QOL, and esophageal acid exposure, while eliminating the need for antisecretory medications in a majority of patients. However, there were no improvements in other physiological measures such as LES pressure, peristaltic amplitude, and LES length. The procedure was well tolerated, with a low rate of self-limited complications. For both studies, limitations included lack of a comparison group, small to moderate sample size, and short to moderate length of follow-up.

A large, retrospective patient registry study (n=558), which involved a diverse group of patients at multiple centers, reported that the Stretta procedure was safe and resulted in significant GERD symptom control and patient satisfaction (Wolfsen and Richards, 2002). Treatment effect was durable beyond 1 year (for 88 patients who were followed beyond 1 year), and most patients were not taking antisecretory medications at follow-up. The limitations included retrospective study design with potential for selection, recall, and other biases, and short follow-up period for the majority of patients. Additionally, there were no data available on objective outcomes, such as esophageal acid exposure, and LES pressure and length.

A randomized, double-blind, sham-controlled, multicenter trial reported that radiofrequency energy delivery significantly improved GERD symptoms and QOL, compared with the sham procedure, at 6 months follow-up, but it did not decrease esophageal acid exposure, LES pressure, or medication use (Corley et al., 2003). Nevertheless, those individuals who were classified as responders, with > 50% reduction in the HRQL score, experienced significant median decreases in 24-hour acid exposure time. In addition to a 13% dropout rate, a greater than anticipated number of sham patients discontinued their medications, and, therefore, the study was underpowered. The study reported only minor transient adverse events. Richards et al. (2003) conducted a prospective study that compared the Stretta procedure with a surgical procedure, laparoscopic fundoplication. Patients were stratified to one or the other procedure according to size of their hiatal hernia, LES pressure, and the presence or absence of significant pulmonary symptoms or Barrett’s esophagus. Both patient groups were highly satisfied and had similar improvements in GERD symptoms and QOL, although follow-up was short term. However, only 58% of Stretta patients were not taking PPI medications post procedure, compared with 97% of surgical patients. More adverse events were reported in the laparoscopic fundoplication group compared with the Stretta group. The authors concluded...
that the Stretta system appears to be a moderately effective and safe alternative to laparoscopic fundoplication in well-selected patients. This comparative study was not randomized, and patients in the Stretta group had less severe disease, potentially biasing the results.

Two prospective studies suggested that the Stretta system was safe and significantly improved GERD symptoms and QOL, while eliminating the need for PPIs in the majority of patients. However, both studies were methodologically flawed, with small sample sizes, no comparison group, and short-term follow-up (Houston et al., 2003; Tam et al., 2003). In addition to the other measures, Tam et al. investigated the effects of radiofrequency energy delivery on mechanisms of spontaneous reflux and reported significant effects on LES function that are associated with improvement in the antireflux barrier, such as the rate of postprandial tLESRs, which was reduced, and postprandial basal LES pressure, which was increased. These effects were associated with a reduction in reflux events and esophageal acid exposure.

Two prospective studies were performed to evaluate the long-term efficacy (4 years) of the Stretta procedure in patients with GERD (Noar and Lotfi-Emran, 2007; Reymunde and Santiago, 2007). Both studies concluded that Stretta was a safe, effective, and durable treatment that improved GERD symptoms and QOL, while reducing medication usage during the 4-year period of follow-up. The studies were uncontrolled and did not include objective outcomes.

In a European, multicenter, open-label, prospective study on the efficacy of the Stretta procedure in the treatment of GERD, investigators focused on objective parameters (esophageal acid exposure, manometry, LES pressure, reflux time and DeMeester score) in addition to medication use, GERD-HRQL and SF-36 scores (Meier et al., 2007). After 12 months, the procedure proved to be well tolerated and effective, with a favorable impact on medication use, LES pressure, esophageal acid exposure, and GERD symptoms scores. This study reported positive objective and subjective outcome measures. Lack of a control group was the most important shortcoming of this study.

Overall, the studies on the Stretta procedure reported improved GERD symptoms, QOL scores, and medication use in all studies. The studies monitoring esophageal acid exposure reported improvement or no effect. The largest study, and the studies with the longest follow-up, did not include this outcome measure.

**EsophyX System with SerosaFuse Fastener:**

The literature search revealed seven prospective, mostly small-sized uncontrolled studies that evaluated the feasibility, efficacy, and safety of transoral incisionless fundoplication using the EsophyX/SerosaFuse system in symptomatic GERD patients. The overall GERD population ranged from a very select to a wide case mix of patients. None of the studies included a control or comparison group. While there were some positive findings, the evidence is inconclusive regarding the subjective and objective efficacy of the procedure or to determine its long-term impact on health outcomes. The available evidence showed that the procedure improved health outcomes in a subgroup of the population by eliminating symptoms, preventing recurrence of symptoms, and reducing or eliminating the need for pharmacologic therapy. In approximately two-thirds of the patients, recurrence of symptoms resulted in reinstitution of pharmacologic therapy. Surgical reintervention (laparoscopic Nissen fundoplication or repeat transoral incisionless fundoplication) was performed in approximately 13% of the overall study population. The evidence of durability of the procedure was limited; two studies evaluated outcomes up to 2 years post transoral incisionless fundoplication. The available evidence showed a rate of serious procedural complications of approximately 6% (14 cases), including esophageal perforations, pleural perforations with
pneumothorax, or intraluminal bleeding events. The overall quality of the evidence is very low since the available studies lack adequate control or comparison groups, and have small populations, and inadequate follow-up times. Additional well-designed, independent comparative clinical trials with long-term follow-up are required to further evaluate the GERD plication procedure using the EsophyX/SerosaFuse system. Future trials need to define which subpopulation may benefit the most from this procedure, the magnitude of the benefits of this procedure, its efficacy relative to other GERD therapies, and its durability since symptom persistence has been problematical with most of the available endoluminal procedures. In addition, future studies must include objective assessment of outcomes such as pH testing and endoscopic evaluation to confirm improvements in health outcomes.

Transesophageal Endoscopic injection and implantation of polymer material:
Five studies involving endoscopic injection and implantation techniques were identified in the published, peer-reviewed literature. Of the three studies that evaluated Enteryx, one was a small pilot study and two were larger, multicenter studies by the same group of investigators who used the same study population and reported results separately after 6 and 12 months of follow-up. The following results were reported for Enteryx:

- Significant improvement in GERD symptoms at 6 months and 12 months.14,16,17 (Johnson and Ganz et al, 2003; Fockens and Bruno et al, 2004).
- Significant improvement in quality of life (QOL) at 6 months and 12 months. (Johnson and Ganz et al, 2003; Fockens and Bruno et al, 2004).
- Significant reduction in esophageal acid exposure at 6 months and 12 months. (Johnson and Ganz et al, 2003).
- Elimination of need for antisecretory medications in most patients.14-16 (Devière and Pastorelli et al, 2002; Johnson and Ganz et al, 2003).
- No significant change in LES pressure. (Devière and Pastorelli et al, 2002).

Only one small prospective study evaluated PMMA implantation in patients followed for 5 to 11 months (mean 7.2 months). (Feretis and Benakis et al, 2001). Results were:

- Significant improvement in GERD symptoms.
- Elimination of need for antisecretory medications in most patients.
- No serious complications; mild transient complications included chest pain, self-limiting bleeding, dysphagia, and gas-bloat syndrome.

Only one study evaluated the Gatekeeper procedure, combining data from two prospective European multicenter trials. (Johnson and Ganz et al, 2003). Results were:

- Significant improvement in GERD symptoms and QOL (physical score only) at 6 months.
- Significant increase in LES pressure at 6 months.
- Significant reduction in esophageal acid exposure at 6 months.
- Data on medication use were not collected systematically at all sites.
- Two serious adverse events (3.0%; pharyngeal perforation and postprandial nausea) occurred, but patients recovered uneventfully; mild complications included sore throat, retrosternal pain, and epigastric pain.
Magnetic sphincter augmentation (MSA) device (LINX Reflux Management System):

Eight studies measured quality of life (QOL) using the GERD-HRQL questionnaire (Bonavina et al., 2008; Bonavina et al., 2010; Lipham et al., 2012; Bonavina et al., 2013b; Ganz et al., 2013; Louie et al., 2014; Ganz et al., 2015; Reynolds et al., 2015a; Reynolds et al., 2015b; Riegler et al., 2015; Saino et al., 2015; Warren et al., 2015). The preoperative GERD-HRQL scores improved after implantation of the MSA device in all studies. Five studies compared GERD-HRQL scores in patients undergoing MSA versus patients undergoing LNF (Louie et al., 2014; Reynolds et al., 2015a; Reynolds et al., 2015b; Riegler et al., 2015; Warren et al., 2015). No statistically significant between-group differences in GERD-HRQL scores in MSA patients versus LNF patients were noted.

Eight studies monitored use of PPIs after implantation of the MSA device (Bonavina et al., 2008; Bonavina et al., 2010; Lipham et al., 2012; Bonavina et al., 2013b; Ganz et al., 2013; Louie et al., 2014; Ganz et al., 2015; Reynolds et al., 2015a; Reynolds et al., 2015b; Riegler et al., 2015; Saino et al., 2015; Warren et al., 2015). All 3 studies evaluating the efficacy of MSA noted a statistically significant reduction in the number of patients using PPIs after MSA. Among comparative studies, results were mixed. One study noted a statistically significant difference in the number of patients using PPIs after MSA compared with LNF, favoring patients who had undergone LNF (Warren et al., 2015). Three cohort studies reported no statistically significant difference in PPI use between MSA and LNF groups (Louie et al., 2014; Reynolds et al., 2015a; Reynolds et al., 2015b). One cohort study reported that patients in the MSA group were statistically significantly less likely to use PPIs at follow-up compared with their counterparts who had undergone LNF (Riegler et al., 2015).

Three studies reported esophageal pH outcomes (Bonavina et al., 2008; Bonavina et al., 2010; Lipham et al., 2012; Ganz et al., 2013; Louie et al., 2014; Saino et al., 2015). In 2 repeated measures time series, pH levels normalized in a majority of patients at follow-up compared with preoperative levels (Bonavina et al., 2008; Bonavina et al., 2010; Lipham et al., 2012; Ganz et al., 2013; Saino et al., 2015). One study compared MSA with LNF (Louie et al., 2014). While patients undergoing MSA had statistically significantly improvements in pH outcomes, differences between groups were statistically significant, favoring LNF.

While MSA implantation appears to be relatively safe, with no major complications or deaths reported in the reviewed studies, dysphagia was a common AE occurring in 3% to 83% of patients in all of the reviewed studies. In 6 studies comparing MSA with LNF, dysphagia at follow-up was comparable between groups (Louie et al., 2014; Reynolds et al., 2015a; Reynolds et al., 2015b; Riegler et al., 2015; Warren et al., 2015). However, 1 comparative study reported that upon occurrence, dysphagia in patients who had undergone MSA was more persistent and severe than in patients who had undergone LNF (Sheu et al., 2015). Specifically, 50% of all MSA patients in this study eventually (within an average of 130 days) required endoscopic dilation compared with 0% in the LNF group.

From 0% to 7% of the patients in the reviewed studies had the MSA device removed for the following reasons: persistent GERD, dysphagia, odynophagia, pain, intermittent vomiting, and magnetic resonance imaging.

In summary, the low-quality body of evidence from 9 studies suggests that MSA may effectively and safely resolve GERD symptoms in patients with PPI-refractory GERD. Studies evaluating the efficacy of MSA demonstrated an overall improvement in outcomes from baseline. Mixed evidence from 6 comparative studies suggests that MSA may be a viable alternative to LNF; however, substantial uncertainty exists. While MSA implantation appears to be relatively safe, with no major complications or deaths reported in
the reviewed studies, dysphagia was a common adverse event (AE) frequently resulting in endoscopic dilation. Unfortunately, no published randomized controlled trials compare laparoscopic MSA with LNF. The eligible studies all have significant methodological limitations, including small sample sizes, high attrition, retrospective nonrandomized study designs, significant between-group differences at baseline in comparative studies, lack of objective assessments (i.e., pH evaluation at follow-up), and lack of a comparison group. The optimal patient selection criteria for MSA as treatment for GERD have not been established. The inclusion criteria in the eligible studies are highly selective, essentially consisting of patients with milder forms of GERD without associated esophageal conditions such as severe esophagitis or large hiatal hernias. There is a lack of data on patients with moderate to severe esophageal disease and moderate to severe obesity, a risk factor for GERD. However, some longitudinal repeated measures time series have reported long-term efficacy with few safety issues. Additional, independent, well-designed comparative studies are needed to confirm long-term safety and effectiveness, to develop management algorithms for patients with post-implantation dysphagia, and to explore health outcomes in a broader patient population in the general clinical setting.

The Angelchik anti-reflux prosthesis: This device was approved (PMA) by the FDA in 1979. It is a soft, collar-shaped, silicone elastomer shell filled with silicone gel, with an internal diameter of 3.1 cm. It is placed around the esophagus under the diaphragm and above the stomach, and is secured by 2 reinforced Teflon straps around the gastro-esophageal junction. The alleged advantage of the Angelchik device is the simplicity of the procedure -- its placement requires only limited dissection, thus decreasing the operating time. Since its introduction, more than 25,000 prostheses have been inserted into patients worldwide. Early faulty design had caused breakage of the circumferential strap, and led to migration of the device. Modification of the original strap to 2 reinforced, non-circumferential straps by the manufacturer appears to have minimized the migration problem. However, complications as a consequence of implantation of the Angelchik prosthesis have been reported in as many as 10 to 20% of patients. An American Medical Association's DATTA evaluation of the Angelchik prosthesis found that this device has not been established as safe and effective for routine use in the treatment of GERD. Long-term studies concluded that the Angelchik device causes long-term dysphagia in many patients, severe enough to require its removal in 25% of these patients. Thus, its continual use cannot be recommended.

1. EXTERNAL SOURCES/ GROUPS POLICY:

Society of American Gastrointestinal and Endoscopic Surgeons (SAGES): In 2009, the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) published a position statement on endoluminal therapies for gastrointestinal diseases. In its statement the Society fully endorsed the evolution of new treatments for gastrointestinal conditions that provide patients with a faster recovery from their procedures while at the same time providing high-quality outcomes (SAGES, 2009). This position statement does not specifically mention the Esophyx device.

American Society of General Surgeons (ASGS): In April 2011, the American Society of General Surgeons (ASGS) published a position statement regarding the use of transoral incisionless fundoplication (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. The Society also supports its use for patients who wish to avoid lifetime drug therapy for this condition. The ASGS 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 of the surgeon, his or her
American Gastroenterological Association: In a monograph published in 2002, the American Gastroenterological Association stated that (1) current endoscopic therapeutic procedures for GERD (which includes endoscopic suturing) are approved for safety, not efficacy, (2) there is currently no adequate randomized clinical trial evidence to support endoscopic therapies, and (3) the public and physicians should be educated about the risk and limitations of endoscopic procedures. This report does not include research evidence published after 2002 or any studies evaluating the Endoscopic Suturing Device/Sew-Right or the Plicator system.

American College of Gastroenterology (ACG): In a 2005 Practice Guidelines for GERD, the ACG recommendations state that endoscopic therapy controls symptoms in selected patients with well-documented GERD. According to the ACG, the techniques seem to improve reflux symptoms, although significant changes in lower esophageal pressure have not been documented. Less than 35% of the patients have demonstrated normalization of their intraesophageal acid exposure, which is measured by ambulatory pH testing. The available published abstracts leave many issues unresolved, including long-term durability, safety and efficacy of endoscopic therapies performed outside of clinical trials with efficacy in atypical presentations of GERD (Devault, 2005).

**APPLICABLE CODES:**

The Current Procedural Terminology (CPT®) codes and HCPCS codes listed in this policy are for reference purposes only. Listing of a service or device code in this policy does not imply that the service described by this code is a covered or non-covered health service. The inclusion of a code does not imply any right to reimbursement or guarantee claims payment. Other medical policies and coverage determination guidelines may apply.

<table>
<thead>
<tr>
<th>HCPCS Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>C9724</td>
<td>Endoscopic full-thickness plication in the gastric cardia using endoscopic plication system (EPS); includes endoscopy</td>
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<table>
<thead>
<tr>
<th>ICD-9 Code</th>
<th>Description</th>
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<tr>
<td>S30.1x*</td>
<td>Esophagitis</td>
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<tr>
<td>S30.11</td>
<td>Reflux esophagitis</td>
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<td>S30.20, S30.21</td>
<td>Esophageal ulceration</td>
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<td>S30.3</td>
<td>Esophageal stricture</td>
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<td>S30.81</td>
<td>Esophageal reflux, gastroesophageal reflux</td>
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<tr>
<td>S30.85</td>
<td>Barrett’s esophagus</td>
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<tr>
<td>S53.3</td>
<td>Hiatal hernia</td>
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* The x represents a range of codes; it is dependent on the specific diagnosis.

<table>
<thead>
<tr>
<th>ICD-10 Code</th>
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<td>Gastro-esophageal reflux disease with esophagitis</td>
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<td>K21.9</td>
<td>Gastro-esophageal reflux disease without esophagitis</td>
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<tr>
<th>CPT® Code</th>
<th>Description</th>
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<tr>
<td>43228</td>
<td>Esophagoscopy, rigid or flexible; with ablation of tumor(s), polyp(s), or other lesion(s), not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique</td>
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<td>43257</td>
<td>Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; with delivery of thermal energy to the muscle of lower</td>
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<tr>
<td>Code</td>
<td>Description</td>
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<tr>
<td>43258</td>
<td>Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; with ablation of tumor(s), polyp(s), or other lesion(s), not amenable to removal by hot biopsy forceps, bipolar cautery or snare technique</td>
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<td>43999</td>
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<td>49999</td>
<td>Unlisted procedure, abdomen, peritoneum and omentum</td>
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<tr>
<td>C9724</td>
<td>Endoscopic full-thickness plication of the stomach using endoscopic plication system (eps); includes endoscopy</td>
</tr>
</tbody>
</table>

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REFERENCES:


38. EndoGastric Solutions (EGS). EsophyX for Patients: TIF®—Transoral Incisionless Fundoplication With EsophyX®. 2011.

60. Hayes Stretta Procedure (Mederi Therapeutics Inc.) for Gastroesophageal Reflux Disease (GERD)


