Clinical Policy Title: Anti-reflux devices for gastroesophageal reflux disease

Clinical Policy Number: 08.03.03

Effective Date: April 1, 2015
Initial Review Date: January 21, 2015
Most Recent Review Date: February 15, 2017
Next Review Date: February 2018

Related policies:
None.

ABOUT THIS POLICY: Keystone First has developed clinical policies to assist with making coverage determinations. Keystone First’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Keystone First when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First will update its clinical policies as necessary. Keystone First’s clinical policies are not guarantees of payment.

Coverage policy

Keystone First considers the use of anti-reflux devices for treatment of gastroesophageal reflux disease (GERD) to be investigational and, therefore, not medically necessary. These devices or techniques include:

- Radiofrequency ablation.
- Sphincter bulking agents.
- Transoral incisionless fundoplication (TIF).
- Endoscopic suturing or stapling.
- Magnetic sphincter augmentation (MSA).

Limitations:

All other uses of antireflux devices for the treatment of GERD are not medically necessary.
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.

Alternative covered services:

- Histamine 2 (H2) blockers.
- Proton pump inhibitors (PPIs).
- Prokinetics (e.g., bethanechol and metoclopramide).
- Antibiotics (e.g., erythromycin).
- Open or laparoscopic Nissen fundoplication (LNF).
- Bariatric surgery (e.g., Roux-en-Y gastric bypass surgery) in obese patients.

Background

GERD is a common health problem for adults, affecting about 20 percent of the U.S. population (El-Serag, 2004). GERD can impact quality of life and is a risk factor for complications, such as Barrett’s esophagus and esophageal adenocarcinoma. GERD results when the lower esophageal sphincter fails to function properly, causing stomach contents to rise up into the esophagus. Anatomic abnormalities such as hiatal hernias, obesity, pregnancy, certain medications, smoking, and inhaling secondhand smoke can contribute to GERD (National Institute of Diabetes and Digestive and Kidney Diseases [NIDDK], 2016).

The main symptom of GERD is frequent heartburn, though some adults with GERD will not experience heartburn (NIDDK, 2016). Other common GERD symptoms include:

- A dry, chronic cough.
- Wheezing.
- Asthma and recurrent pneumonia.
- Nausea.
- Vomiting.
- A sore throat, hoarseness, or laryngitis.
- Difficulty swallowing or painful swallowing.
- Pain in the chest or the upper part of the abdomen.
- Dental erosion and bad breath.

Lifestyle changes and anti-reflux medications are often the initial treatments for suspected GERD
If symptoms improve with these treatment methods, a GERD diagnosis often does not require testing. Persistent symptoms and swallowing difficulties may require testing to confirm a diagnosis. Several tests can help with diagnosis. These include upper gastrointestinal (GI) series, esophagogastroduodenoscopy, esophageal pH monitoring, and esophageal manometry.

**Advanced treatment options:**

Medical treatment involves acid suppressants. The most effective and commonly prescribed acid suppression medications are PPIs. Long-term PPI use is associated with increased risk of enteric infections (e.g., Clostridium difficile-associated diarrhea), community-acquired pneumonia, bone fracture, nutritional deficiencies, and interference with metabolism of antiplatelet agents.

Surgery may be indicated for persons with persistent symptoms who fail to respond symptomatically to aggressive acid suppression therapy or who require high doses of PPIs to control symptoms, particularly in young patients who may require lifelong therapy (Kahrilas, 2008). The primary surgical alternative is open or LNF (Society of American Gastrointestinal and Endoscopic Surgeons [SAGES], 2010). Despite the efficacy of surgery, LNF is invasive and carries procedure morbidity, such as dysphagia, gas bloat, and modest long-term durability. Revisional fundoplication may be required for persistent reflux symptoms, dysphagia, or herniation; it is considerably more complicated and is associated with a higher perioperative risk. Given these issues, there is interest in developing an intermediate option as an alternative to chronic prescription drug use, without the morbidity related to surgery.

Endoscopic therapies have emerged to bolster the anti-reflux properties of the gastroesophageal junction (GEJ) to reduce the occurrence of reflux, and several have been approved by the U.S. Food and Drug Administration (FDA) (FDA, 2016). These therapies can be categorized mechanistically into four groups (Katz, 2013):

- Radiofrequency ablation to the lower esophageal sphincter (LES).
- Injectable bulking agents into the LES.
- Endoscopic suturing.
- TIF, which is a suturing technique designed to create a full thickness gastroesophageal valve from inside the stomach.

MSA, also referred to as magnetic esophageal ring implantation, uses a device constructed of magnetic titanium beads connected together with independent titanium wires that is implanted at the LES. Each magnetic bead works independently of the others, allowing physiological movement of the esophagus without tension. The magnetic forces of the beads form a circular unit that holds the LES closed, and the titanium wires allow the device to expand. Intraoperative measurements are obtained to determine device size and resistance to expansion needed to augment LES function. Unlike other laparoscopic anti-reflux procedures, MSA does not alter gastric anatomy and can be explanted if necessary. Implantation requires approximately 30 minutes and may be performed on an outpatient basis.
Searches

Keystone First searched PubMed and the databases of:
- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality's National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on December 14, 2016. Search terms were: “GERD,” “reflux,” “anti-reflux,” “fundoplication,” “Stretta,” “Esophyx,” “Enteryx,” “endoscopic plication system,” “endoCinch,” and “transoral incisionless fundoplication.”

We included:
- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews**.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

Findings

We identified four systematic reviews (Hayes, 2015a and b; Lipka, 2015; Wendling, 2013); one cost-effectiveness study (Funk, 2015); and several evidence-based guidelines for this policy. Multiple new endoluminal devices and therapies have been developed to create a more effective antireflux barrier in patients with chronic GERD, who are unsatisfied or unresponsive to maximal antireflux medical therapy or who refuse LNF. However, many devices have been abandoned because of ineffectiveness or significant adverse effects (Hayes, 2015a).

The systematic reviews and meta-analyses assessed the evidence for the following FDA-approved antireflux devices:
- Radiofrequency ablation using the Stretta® procedure (Mederi Therapeutics Inc., Norwalk, Connecticut).
- Sphincter bulking agents using ENTERYX® (Boston Scientific, Marlborough, Massachusetts), subsequently withdrawn from the market.
- TIF using Esophyx® (EndoGastric Solutions Inc., Redmond, Washington).
- Endoscopic suturing or stapling using the Medigus Ultrasonic Surgical Endostapler (MUSE™) (Medigus USA, Danville, California)
The safety, efficacy, durability, and cost-effectiveness of endoscopic therapies relative to conventional pharmacologic or surgical treatment of GERD have not been established in the published medical literature. Current studies are generally of small to moderate size, lack adequate control or comparison groups, and provide only short-term follow-up. The effectiveness of these devices is modest compared with sham procedures in high-quality studies, and the risks have either been too great or inadequately studied compared with fundoplication. Well-designed clinical trials with long-term follow-up are required to establish that endoscopic therapies benefit health outcomes in patients with GERD by eliminating symptoms, preventing recurrence of symptoms or progression of disease, healing esophagitis, and reducing or eliminating the need for pharmacologic therapy.

Evidence-based guidance from the National Institutes for Health and Clinical Excellence (NICE) (2011 and 2013), the SAGES (Auyang, 2013), the American Society for Gastrointestinal Endoscopy (ASGE) (2015), and the American College of Gastroenterology (ACG) (Katz, 2013) concur with these findings with two exceptions. SAGES issues a strong recommendation for using the Stretta procedure for patients with GERD who are ≥18 years of age, with persistent symptoms of heartburn, regurgitation, or both for ≥six months, have been partially or completely responsive to pharmacologic therapy, and have declined LNF. ASGE suggests endoscopic antireflux therapy for selected patients with uncomplicated GERD, after careful discussion with the patient regarding potential adverse effects, benefits, and other available therapeutic options.

The American Society of General Surgeons (ASGS) supports the use of either transoral fundoplication using multiple fasteners or TIF at the discretion of the general surgeon for patients who are candidates for surgical fundoplication (ASGS, 2016). Their rationale is that the transoral procedure is a suitable minimally invasive option, as long as it adheres to the same fundamental surgical principle of creating a full thickness esophagogastric fundoplication to correct an incompetent LES. However, limited evidence supports their decision.

There is insufficient evidence to support the use of MSA for the treatment of GERD. The evidence consists of industry-sponsored studies of low quality with a high risk of bias. Results suggest MSA may effectively and safely resolve the symptoms and be a viable alternative to LNF in certain patients, but there is considerable uncertainty in the findings. The optimal patient selection criteria have not been established. Study inclusion criteria were highly selective, consisting primarily of patients with milder forms of GERD who had at least some response to PPI therapy without associated esophageal conditions such as severe esophagitis or large hiatal hernias. The available evidence does not support extending MSA application to patients with hiatal hernia larger than three centimeters (cms).

The FDA mandated two post-approval studies to evaluate the long-term safety and effectiveness of MSA and the incidence of adverse events (FDA, 2016). At one-year follow-up, there were no device migrations or malfunctions and no events leading to long-term complications or deaths. Device removal occurred in 3.4 percent of patients, mainly due to dysphagia followed by recurrent symptoms of GERD. A five-year follow up study is ongoing (clinicaltrials.gov identifier NCT01940185).
Evidence-based guidelines vary in their support for MSA. The ACG found limited evidence that MSA provided consistent, durable symptom relief and pH control with markedly fewer side effects than traditional LNF in highly selected patients for up to four years (Katz, 2013). However, more data are required before widespread usage can be recommended. ASGS supports the LINX procedure as a mechanism for controlling GERD when it is placed by properly trained laparoscopic surgeons with experience in foregut surgery and management of GERD (ASGS, 2014). The SAGES guideline makes no mention of MSA (SAGES, 2010).

**Policy updates:**

None.

**Summary of clinical evidence:**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASGS (2016)</td>
<td>Key points:</td>
</tr>
<tr>
<td>Position statement: transoral fundoplication</td>
<td>• Supports the use of either transoral fundoplication using multiple fasteners or TIF at the discretion of the general surgeon for patients who are candidates for surgical fundoplication.</td>
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<td></td>
<td>• The transoral procedure is a nonsurgical option as long as it creates a full-thickness esophagogastric fundoplication to correct an incompetent LES.</td>
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<td></td>
<td>• Based on limited evidence.</td>
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<td>ASGE (2015)</td>
<td>Key points:</td>
</tr>
<tr>
<td>Role of endoscopy in the management of GERD</td>
<td>• Committee suggests considering endoscopic antireflux therapy for selected patients with uncomplicated GERD after careful discussion with the patient regarding potential adverse effects, benefits, and other available therapeutic options.</td>
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<td>Funk (2015)</td>
<td>Key points:</td>
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<tr>
<td>Cost effectiveness of medical, endoscopic, and operative treatments for adults with GERD who require daily PPI therapy.</td>
<td>• Markov model was generated from the payer’s perspective using a six-month cycle and 30-year time horizon; parameters selected using the published literature and institutional billing data.</td>
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<td>• Four treatment strategies were analyzed: PPI therapy, TIF (EsophyX), radiofrequency ablation (Stretta), and LNF.</td>
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<td>• Base case analysis assumed a PPI cost of $234 over six months ($39 per month).</td>
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<td>• Stretta and LNF were the most cost effective ($2,470.66 and $5,579.28 per quality-adjusted life-year gained, respectively).</td>
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<td>• If PPI therapy &gt; $90.63 per month over 30 years, LNF was dominant.</td>
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<td>• LNF was more cost effective than EsophyX at all points in time.</td>
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<tr>
<td>Hayes (2015, updated 2016)</td>
<td>Key points:</td>
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<tr>
<td>Endoscopic therapy for GERD</td>
<td>• Systematic review of 10 comparative and five noncomparative studies (nine of Stretta, four of EsophyX, two of MUSE).</td>
</tr>
<tr>
<td>Citation</td>
<td>Content, Methods, Recommendations</td>
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<td>Overall quality: very low (MUSE) to low (Stretta, EsophyX) due to limited number of studies, lack of randomization or blinding, and short follow-up (six months to one year). Improved clinical and patient-reported outcomes from baseline for Stretta and EsophyX for patients who are unsatisfied with or uncontrolled on PPIs. Stretta and EsophyX are generally safe, with mild to moderate side effects. Insufficient evidence regarding the effectiveness and safety of MUSE. Compared to LNF, all three procedures had significantly lower procedure times and shorter lengths of stay. Contraindications for each device were specified in FDA labeling.</td>
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<tr>
<td>Hayes (2015, updated 2016) MSA (LINX) for GERD</td>
<td>Key points:</td>
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<tr>
<td>Systematic review of nine studies (one prospective cohort study, five retrospective cohort studies, two repeated measures time series, and one case series). No randomized controlled trials (RCTs) found. Overall quality: low with a high degree of uncertainty. Mostly industry-sponsored studies and included highly selected patients with milder forms of GERD without associated esophageal conditions such as severe esophagitis or large hiatal hernias. Results from single arm series showed MSA is safe and improved quality of life, reduced PPI use, and normalized pH. Comparative studies showed mixed results or results favoring LNF. 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.</td>
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<td>Lipka (2015) Stretta for the management of GERD</td>
<td>Key points:</td>
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<td>Systematic review and meta-analysis of four RCTs (165 total patients). Three trials compared Stretta versus sham, and one trial compared Stretta versus PPI therapy. Overall quality: very low. No difference between Stretta versus sham or PPI therapy for the outcomes of mean time spent at a pH &lt; 4 over a 24-hour time course, LES pressure, ability to stop PPIs, or health-related quality of life (HRQOL).</td>
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<td>ASGS (2014) Position statement on LINX</td>
<td>Key points:</td>
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<tr>
<td>Supports the LINX procedure as mechanism for controlling GERD when it is placed by properly trained laparoscopic surgeons with experience in foregut surgery and the management of GERD patients.</td>
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<td>Auyang (2013) for SAGES Guidance: endoluminal treatments for GERD</td>
<td>Key points:</td>
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<td>EsophyX: In short-term follow-up, from six months to 2 years, EsophyX may be effective in patients with hiatal hernia 2 cm with typical and atypical GERD. Long-term data are unavailable. Further studies need to define optimal techniques, patient-selection criteria, and device/technique safety. (Low quality of evidence; weak recommendation.) Stretta recommended for patients with GERD who are ≥ 18 years of age, with persistent symptoms of heartburn, regurgitation, or both for ≥ six months; have been partially or completely responsive to pharmacologic therapy; and have declined LNF (high quality of evidence; strong recommendation).</td>
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<td>Citation</td>
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| Katz (2013) for the ACG Guidance: diagnosis and management of GERD | Key points:  
- Stretta not recommended for patients with severe esophagitis, long-segment Barrett’s esophagus, dysphagia, hiatal hernia > 2 cm, autoimmune disease, collagen vascular disease, and/or coagulation disorders.  
- Endoscopic therapies for GERD have not demonstrated long-term efficacy.  
- Do not recommend current endoscopic therapy or TIF as an alternative to medical or traditional surgical therapy. (Conditional recommendation, moderate level of evidence.) |
| NICE (2013) Guidance: radiofrequency ablation | Key points:  
- Endoscopic radiofrequency ablation for GERD is safe in the short and medium terms, but longer-term outcomes are unclear.  
- Achieves symptomatic relief, but objective evidence on reduction of reflux is inconclusive.  
- Procedure should only be used with special arrangements for clinical governance, consent, and audit or research. |
| Wendling (2013) TIF | Key points:  
- Systematic review of 15 studies reporting on over 550 procedures.  
- TIF significantly reduced both GERD-HRQOL scores (21.9 versus 5.9, p < 0.0001) and Reflux Symptom Index scores (24.5 versus 5.4, p ≤ 0.0001).  
- Overall patient satisfaction = 72%.  
- PPI discontinuation rate = 67%, with a mean follow-up of 8.3 months.  
- pH metrics were not consistently normalized.  
- Major complication rate = 3.2%; failure rate = 7.2%.  
- TIF effectiveness and durability, and optimal patient population are not determined. |
| NICE (2011) Guidance: endoluminal gastroplication (TIF) | Key points:  
- No major safety concerns.  
- RCTs suggest some short-term reduction in medication requirement, but other outcomes are inconsistent, sustained improvement in esophageal pH measurement is not demonstrated.  
- TIF should only be used with special arrangements for clinical governance, consent, and audit or research. |

**References**

**Professional society guidelines/other:**


**Peer-reviewed references:**


**CMS National Coverage Determinations (NCDs):**

No NCDs were identified as of the writing of this policy.


A52893 Non-coverage of Transoral Incisionless Fundoplication. CMS website.
A55330 Self-administered drug (SAD) list revision to the Part A and Part B article. CMS website.

Local coverage determinations (LCDs):


Commonly submitted codes

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

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<th>CPT Code</th>
<th>Description</th>
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<tr>
<td>43210</td>
<td>Transoral incisionless fundoplication (TIF)</td>
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<td>K21.0</td>
<td>Gastro-esophageal reflux disease with esophagitis</td>
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<tr>
<td>K21.9</td>
<td>Gastro-esophageal reflux disease without esophagitis</td>
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<th>Description</th>
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