



BlueCross BlueShield
of Alabama

Name of Policy:

**Transesophageal Endoscopic Therapies for Gastroesophageal
Reflux Disease-GERD**

Policy #: 023
Category: Surgery

Latest Review Date: December 2013
Policy Grade: B

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

- 1. The technology must have final approval from the appropriate government regulatory bodies;*
- 2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
- 3. The technology must improve the net health outcome;*
- 4. The technology must be as beneficial as any established alternatives;*
- 5. The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

- 1. In accordance with generally accepted standards of medical practice; and*
- 2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
- 3. Not primarily for the convenience of the patient, physician or other health care provider; and*
- 4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

Transendoscopic therapies for the treatment of gastroesophageal reflux disease have been developed in recent years primarily due to the high prevalence of this condition. These treatments are considered a minimally invasive therapeutic alternative to the open laparoscopic fundoplication or chronic medication therapy. This type of procedure may be considered Natural Orifice Transluminal Surgery (NOTES). This review describes several different procedures.

The first procedure is the transesophageal endoscopic gastroplasty, also referred to as gastroplication, fundoplication or transoral incisionless fundoplication (TIF). This is usually an outpatient procedure under local anesthesia, which takes 30-35 minutes. Sutures or fasteners are placed in the lower esophageal sphincter during this procedure to strengthen and lengthen the sphincter to assist with decreasing the reflux.

Currently, three endoscopic suturing devices have received FDA 510(k) marketing clearance for use in the treatment of GERD:

1. EndoCinch™ (CR Bard) is a suture technique for partial-thickness plication, cleared in January 2001.
2. NDO Plicator™ (Ethicon Endo-Surgery) for full-thickness plication, cleared in May 2003.
3. EsophyX™ (EndoGastric Solutions) for full-thickness plication, cleared in September 2007.

The StomaphyX device has broader FDA clearance for use in endoluminal tissue approximation and ligation in the gastrointestinal tract.

The second procedure is a transesophageal procedure in which radiofrequency thermal lesions are created in the lower esophageal sphincter. Radiofrequency (RF) energy has been used to produce submucosal thermal lesions at the gastroesophageal junction. (This technique has also been referred to as the Stretta procedure. The CSM Stretta® System [Conway Stuart] received 510(k) marketing clearance from the FDA in 2000 for general use in the electrosurgical coagulation of tissue and is specifically intended for use in the treatment of GERD. Stretta® is currently manufactured by Mederi Therapeutics, Greenwich, CT.) Specifically, radiofrequency energy is applied through four electrodes inserted into the esophageal wall at multiple sites both above and below the squamocolumnar junction. The mechanism of action of the thermal lesions is not precisely known but may be related to ablation of the nerve pathways responsible for sphincter relaxation or may induce a tissue-tightening effect related to heat-induced collagen contraction.

The third procedure is injection or implantation of biocompatible polymers. Implantation of a biocompatible polymer (Enteryx™), which can be injected into the lower esophageal sphincter, has also been investigated. In addition, the endoscopic submucosal implantation of polymethylmethacrylate beads has been studied as a method to reduce GERD symptoms when injected into the lower esophageal folds.

The polymer, Enteryx™, received FDA approval in 2003 through the premarket approval (PMA) process for the treatment of symptomatic GERD. However, on September 23, 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.

As another possible bulking agent, Pyrolytic carbon-coated zirconium oxide spheres (Durasphere®), is being evaluated. Durasphere® is a bulking agent approved for treatment of urinary and fecal incontinence. Use of this product for esophageal reflux would be considered off-label use. The website of Carbon Medical Technologies states that Durasphere GR is an investigational device in the U.S. “intended to treat problems associated with GERD.”

The Gatekeeper Reflux Repair System (Medtronic, Shoreview, MN) 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.

The Plicator™ is a flexible endoscopic instrument that is passed into the stomach in conjunction with a flexible gastroscope. The Plicator is used to grasp and fold the gastric cardia, fixating it with a transmural suture-pledget. The resulting full-thickness tissue plication restructures the gastro-esophageal flap valve, enhancing the mechanical functioning of the body’s natural anti-reflux barrier. The Plicator procedure is performed under moderate sedation, typically in 20 minutes, enabling patients to return home the same day. The Plicator received FDA clearance in 2003.

Policy:

Endoscopic gastroplasty or gastroplication does not meet Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered **investigational** for the treatment of gastroesophageal reflux disease.

The **Stretta procedure or radiofrequency of the lower esophageal sphincter does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered **investigational** when used as a treatment for gastroesophageal reflux disease.

The **implantation of polymers, spheres, or injection of beads into the lower esophageal sphincter does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered **investigational**.

The **implantation of a prosthesis or hydrogel does not meet** Blue Cross and Blue Shield of Alabama’s coverage criteria and is considered **investigational**.

The **fixation of a transmural suture-pledget (Plicator procedure) for the treatment of gastroesophageal reflux diseases does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage and is considered **investigational**.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

Endoscopic Plication

There are two studies that reported results of endoscopic plication using non-FDA approved devices. Swain (1999) reported on a case series of 28 patients with GERD whose symptoms were not controlled with medical therapy and who were offered and declined open or laparoscopic antireflux surgery, or who were considered unfit for anesthesia due to concurrent illness. Therefore, in this case, transesophageal suturing appears to be an alternative to surgery, rather than medical therapy. Pre- and postoperative assessment (at three months) focused on symptoms, manometry, and 24-hour ambulatory pH monitoring. There was a significant decrease in symptoms, use of proton pump inhibitors (PPIs), and percentage of time when a pH of less than four was recorded. In addition, there was a significant increase in the length of the lower esophageal sphincter and sphincter pressure. The potential benefits of the procedure noted by the authors include easy repeatability, reversibility, short operation time, and lack of need for general anesthesia. Filipi et al (2001) reported on a multicenter trial of 64 patients who were treated for their GERD with an endoscopic suturing device. The inclusion criteria were three or more heartburn episodes per week while not taking medication, dependency on antisecretory medicine, and documented acid reflux by pH monitoring. It is noted that there is no documentation whether the dependency on the medication controlled the patient's GERD or if it was not affected. Exclusion criteria were dysphagia, grade 3 or 4 esophagitis, obesity, and hiatus hernia greater than 2cm in length. Patients underwent manometry, endoscopy, 24-hour pH monitoring, and symptom severity scoring before and after each endoscopic suturing procedure. Surgical procedures were split into two arms based on a linear or circumferential plication configuration. It was noted that there was no adverse procedural affects recorded. Results were analyzed for a mean of six-month period of time. Heartburn severity as well as regurgitation improved as documented by a P value >0.0001 for each score. Twenty-four-hour pH monitoring demonstrated improvement in the number of episodes below a pH of 4 and a P value <0.0002. Plication configuration did not seem to affect symptoms or pH monitoring results. Adverse effects recorded were noted as procedural rather than device related. There were two esophageal mucosal injuries secondary to overtube placement. Esophageal microperforation occurred in one episode, which resulted in hospitalization of the patient. These case series were evaluated by the 2003 TEC Assessment, which concluded that these types of studies were insufficient to permit conclusions about the effects of transesophageal suturing on GERD. Randomized, controlled trials (RCTs) were needed to determine the comparative impact on outcomes compared to alternatives, and long-term follow-up data were needed.

EndoCinch

In 2006, Montgomery reported on a double-blind sham study of 46 patients with GERD who required daily PPI therapy. In this study, 22 patients had plication (EndoCinch) and 24 had a sham procedure. There were no statistically significant differences between groups for some key measures including acid exposure and discontinuation of PPI. Also, there were no changes in the extent of esophagitis. Also noted was a marked loss of sutures with 67% remaining at 12 months. While the sample size is small, this blinded randomized study highlights many open questions about use of this technique.

In 2007, Schwartz reported on a single-center study of 60 patients with GERD; 20 patients were randomized to EndoCinch; 20 had a sham procedure; and 20 had observation. At three-month follow-up; while PPI use decreased more in the active treatment group (compared to sham), there was no difference between the two groups in acid exposure time. Acid exposure times normalized in 29% of actively treated patients and 22% of sham patients ($p=0.71$). During the 12-month follow-up, 29% of those who received suturing were retreated.

In 2006, Mahmood reported on a nonrandomized contemporaneous comparative study of 27 patients receiving endoscopic plication with Endocinch to 24 patients having laparoscopic Nissen fundoplication (LNF). Many of those receiving endoscopic procedures were referred to a gastroenterologist while those having the fundoplication were often referred directly to a surgeon. Patients had GERD symptoms requiring continuous PPI treatment; some had breakthrough symptoms on PPIs. In this small, non-randomized study, symptom control improved in both groups but was better for the LNF group. Dysphagia was more common after LNF. Ninety-one percent of LNF patients achieved normal esophageal pH compared to 48% in the endoscopic group.

Plicator

Rothstein et al (2006) reported on use of full-thickness plication (Plicator) with three-month follow-up in a randomized, sham-controlled multi-centered study of 159 patients with GERD requiring maintenance therapy. In this short-term study, complete cessation of PPI therapy was higher among those in the treatment group than in the sham group (50% vs. 24%). Quality of life scores also improved more in the active group. The percent reduction in median percent time the pH was less than four was improved more in the active group (7% vs. 10%) but did not change in the sham group (10% vs. 9%). The authors noted that the single full-thickness plication normalized the distal esophageal acid contact for less than one third of the patients and was not effective in healing esophagitis. Also, radiating shoulder pain and abdominal pain were more frequent adverse events in the active treatment group (12% vs. 0% and 9% vs. 0%, respectively).

The results produced a discussion in the article stating that the Plicator procedure shows promise as a treatment option for patients with mild GERD seeking an alternative to long-term acid-suppressive therapy. In addition, information is needed on the long-term durability the effect on clinical outcomes. The authors summarized that endoscopic full-thickness plication with the Plicator was effective in significantly reducing GERD symptoms, medication use, and esophageal acid exposure. In an editorial on this article, Shaheen stated there are issues to be dealt with concerning the acceptance of endoscopic anti-reflux devices such as safety, efficacy

and durability. In regards to the study, Shaheen also states that some head-to-head data with alternative treatment measure would be helpful. No study has truly compared the results of PPI therapy to endoscopic anti-reflux devices. Shaheen concludes his editorial by saying that the study still leaves uncertainty as to where to position endoscopic anti-reflux procedures in the patient with GERD. Since there is a lack of data, there is no claim to superiority, or even equivalency, of these devices to the best medical or surgical therapy for GERD.

Pleskow et al (2006) published a study of 29 patients who complete a 36 month follow-up after a single full-thickness plication in the gastric cardia 1 cm below the gastroesophageal (GE) junction. Treatment effect remained stable from 12 to 36 months, with 21/29 patients off PPI at 12 months compared to 17/29 patients at 36 months. The proportion of patients achieving a $\geq 50\%$ improvement in GERD-HRQL score was consistent from 12 months (59%) to 36 months (55%).

Injection/Implantation of Prosthetics or Bulking Agents

Enteryx

Johnson et al performed the study, which was used for the FDA approval of Enteryx. This was a prospective case series of 55 patients with GERD who were controlled by medical therapy including PPI's. A successful outcome was defined as elimination of PPI use or reduction of PPI use to at least 50% of baseline. Based on this, the therapy was investigated as an alternative to medical therapy. While results indicated that at 12 months, 80.3% of the study subjects met the primary outcome, randomized studies are required to determine treatment effectiveness. The FDA has required a sham-study as part of the post-marketing phase of Enteryx. The long-term efficacy of the implant remains unknown. More than 40% of the subjects had greater than 25% reduction in implant volume at six and 12 months. In addition, 22% of the patients required repeat injection in the first three months after initial injection due to lack of effectiveness or sloughing of implant material.

Three additional studies have been published in 2005 regarding the use of Enteryx; these publications were sponsored by Boston Scientific, the company that manufactures the Enteryx implant device. The study by Cohen et al summarizes that the precise role of Enteryx implantation in treatment of patients with GERD remains to be determined. Since the results of the open-label of trials with Enteryx are promising but more research with this technology is necessary. Devière et al states there was evidence of a substantial placebo effect. By three months, 53% of the sham group had reduced the PPI use $\geq 50\%$ and 22% had sustained improvement. It also states in this article that despite improved symptoms, significant within group or overall reduction in acid exposure could not be detected. Lack of a reduction in acid exposure leaves the question of the mechanism of action of the Enteryx implantation.

In September 2005, Enteryx was voluntarily removed from the Market due to serious adverse effects.

Bulking Agents

Lehman et al (2003) reviewed the injectable and bulk-forming agents used for enhancing the lower esophageal sphincter. He concludes these procedures are "still new, have accumulated limited outcome data, and have not been studied in head-to-head comparison trials." He states

the future utility of these treatments “will become apparent when sound data from well-controlled clinical trials and procedural databases are available.”

In the study by Feretis et al (2001), PMMA was injected by a transesophageal submucosal injection. This was a case series of 10 patients with GERD who were refractory to or dependent on PPIs. While a significant decrease in symptom scores was noted, the post treatment follow-up was not specified by a specific time period. In addition, the small number of patients and lack of long-term follow-up precludes adequate scientific analysis.

Transesophageal Radiofrequency – The Stretta Procedure

Corley et al published results of a randomized, double-blinded, sham-controlled trial of radiofrequency energy applied to the gastroesophageal junction for the treatment of GERD. This trial’s primary endpoints were reflux symptoms and quality of life. Secondary endpoints measured at 0, 6, and 12 months included medication use and esophageal acid exposure. The study found that radiofrequency energy to the gastroesophageal junction significantly and substantially improved GERD symptoms and improved general quality of life at 6 months compared with the sham procedure. Active treatment, however, did not reduce medication use or esophageal acid exposure when compared with the sham procedure. In reviewing Corley’s publication, Hogan, et al, states, “The overall effectiveness of the radiofrequency ablation technique for preventing GERD has not been substantiated, compared with placebo, in this first appropriately designed randomized, controlled clinical trial”.

Triadafilopoulos (2004) provided a study which compared “responders” versus “non-responders” of changes in acid exposure. This proposes is a possible mechanism of action but does not provide evidence on the efficacy of the procedure. Torquati, et al (2004), reports on 41 patients in a case series of 82 patients who had greater than 18 month’s follow-up. No comparative data was reported in this study. A case series is also reported evaluating 50 patients pre- and post-intervention at 3-32 months.

Considering the large patient population which would be affected by GERD, rigorous controlled trials enrolling large number of patients with adequate follow-up are needed. In addition, evidence is needed from rigorously controlled comparisons with other effective treatments of GERD such as the Nissen fundoplication or optimal medical management in order to better characterize the comparative risk and benefits of the Stretta procedure compared to these treatments.

In an endoscopic therapy review for GERD published by David A. Johnson, it states related to Stretta, “However in sharp opposition to this FDA statement, the recent (and only) systemic review of the literature on Stretta concluded; “clear indications for Stretta treatment are nil because of the paucity of controlled data available, patients and the confusing nature of the data that are available”. This was referenced from the article written by Kahrilas and published in *Gastrointestinal Endoscopy* 2003.

February 2010 Update

A literature search was conducted and no new randomized controlled trials addressing the issues outlined above were identified. The 2008 Medical Position statement of the American

Gastroenterological Association make no recommendation for or against “the use of currently commercially available endoluminal antireflux procedures in the management of patients with an esophageal syndrome” based on insufficient evidence (Grade Insufficient).

Transesophageal Suturing

At present, commercially available devices for endoluminal plication are EsophyX and EndoCinch. Cadière et al (2008) reported on an industry-sponsored cohort study of full-thickness (i.e., muscularis) fundoplication (EsophyX) in 86 PPI-dependent GERD patients reported that 68% of patients discontinued PPI medication use at 12 months. Health-related quality of life scores and heartburn scores were significantly different from pre-procedure scores off PPI, but not significantly different from pre-procedures on PPI. Serious adverse events consisted of two esophageal perforations and one case of postoperative intraluminal bleeding requiring transfusion. Birk et al (2009) reported on full-thickness fundoplication using the Plicator in a cohort study of 131 patients who were variably responsive to PPI therapy. At 12 months, 50 patients (38%) were lost to follow-up or had not yet reached their 12 month follow-up visit. Sixty-six percent of the remaining 81 patients demonstrated a 50% reduction in the GERD-Health Related Quality of Life (GERD HRQoL) score compared to their pre-fundoplication (off meds) score. No serious adverse events were reported. The lack of a contemporaneous control (comparison) group greatly limits the use of these findings as noted with previous uncontrolled studies. These case series provide insufficient evidence of overall improved outcomes for patients.

Radiofrequency Energy

Coron et al (2008) reported on an unblinded randomized trial in which 43 PPI-dependent GERD patients either continued the effective dose of their PPI or received the radiofrequency procedure (Stretta, currently manufactured by Mederi Therapeutics). At six months, significantly more patients in the treatment group were able to discontinue or decrease their PPI use by at least 50% than in the control group, a difference that was not maintained at 12 months. However, some authors have suggested that PPI discontinuation rather than dose reduction is a more meaningful outcome measure. In this study, the number of patients able to discontinue PPI medication did not differ between groups. Adverse events in the treatment group were described as “transient” and included abdominal pain or epigastric discomfort, odynophagia, and fever. There were no adverse events in the control group.

Radiofrequency has been applied as supplementation to EndoCinch plication to reduce the loss of mucosal sutures seen at one year with that procedure. Mosler et al (2008) conducted a pilot study in 16 GERD patients comparing endoluminal gastroplication with EndoCinch alone to EndoCinch with cautery of mucosal surfaces prior to suturing. After one year, 10 of 27 sutures (37% in nine patients treated with cautery remained intact, while three of 20 sutures (15%) in seven patients treated with EndoCinch alone remained intact. Initial improvements in heartburn, pH score and medication use were seen at 12 months but were not sustained at 24 months in either group.

Radiofrequency for GERD-associated gastroparesis was assessed in a one-year prospective case series of 31 patients published by Noar et al (2008). At six months, 23 patients (74%) experienced normalization of gastric emptying. Among this group, GERD-HRQoL and

dyspepsia symptoms showed significant improvement from baseline (on medication) at 12 months. Minor complications resolved only GERD-HRQoL remained significantly different from baseline (on medication) at 12 months. Minor complications resolved without sequelae and included four cases of dyspepsia and one case of minor gastric bleeding. There were no serious complications.

Injection of Polymer

No human studies of polymethylmethacrylate implantation for the treatment of GERD were identified. One open-label pilot study of just 10 GERD patients injected Durasphere (Carbon Medical Technologies), a bulking agent approved for treatment of urinary and fecal incontinence, at the gastroesophageal junction. At 12 months, seven patients (70%) discontinued all antacid medication completely. No erosion, ulceration, or sloughing of material was noted at any injection site.

August 2010 Update

A systematic review of 33 studies examined seven endoscopic treatments for GERD (three of which do not have FDA marketing clearance for use in the U.S.). The review included the sham-controlled and active-controlled studies cited above for the EndoCinch suturing system, the Stretta radiofrequency procedure, and the (recalled) Enteryx polymer injection. The authors conclude:

“Despite the potential benefits of these procedures, there is insufficient evidence at present to establish their safety and efficacy, particularly in the long-term.”

Transesophageal Endoscopic Gastroplasty

Three case series of the EsophyX procedure and one case series of the Plicator describe improvement of symptoms, medication use, and quality of life. Measures of acid exposure were variable and revealed inconsistent results. Chen et al., authors of the systematic review cited above, highlight the importance of both subjective and objective improvements in GERD studies: To the extent that improved subjective outcomes are mediated by interruption of submucosal sensory fibers from the vagus nerve, ongoing acid reflux may be undetected, leading to adverse consequences.

Two-year follow-up results from an industry-sponsored feasibility study of the EsophyX procedure included 14 of 19 patients from the original case series. Two patients were excluded from the original study due to gastric anomalies, two patients underwent surgical treatment or repeat endoscopic gastroplasty, and one patient was lost to follow-up. All patients had proton-pump inhibitor (PPI)-dependent GERD for more than six months (median = 10 years). At two years, ten patients (71%) had discontinued daily PPI therapy. GERD-Health-Related Quality of Life (HRQL) scores improved from a median of 17 at baseline *on* PPIs to seven post-treatment, a statistically significant improvement ($p=0.004$). GERD-HRQL scores <12 (indicative of heartburn elimination) were reported by 13 patients (93%). pH scores normalized in all patients, regardless of clinical response to treatment. Small hiatal hernias (< 3 cm) were eliminated in six of ten patients (60%) who had hernias at baseline. Although patients reported transient pharyngeal irritation, bloating, and mild epigastric pain at the time of the procedure, no adverse procedure-related events were reported at two-year follow-up.

Two case series from Milan, Italy studied 20 patients each. A six-month case series enrolled 20 consecutive patients with PPI-dependent GERD over 18 months. This study utilized a new (2.0) version of the EsophyX device that deploys fasteners starting at the posterior and anterior sides of the gastroesophageal valve rather than at the middle of the valve. Eighteen patients, who had pathological gastroesophageal reflux before the procedure, as measured by pH-impedance, were included in the outcomes analysis; two patients with normal 24-hour pH-impedance at baseline were excluded. At six months, ten of the 18 patients (56%) had discontinued daily PPI therapy. GERD-HRQL scores improved from a mean of 45 at baseline *off* PPI to 16 post-treatment, a statistically significant improvement ($p < 0.001$). However, the post-treatment value did not appear to be different from the baseline score *on* PPI, 20. There were significantly fewer acid and non-acid refluxes. There was no significant difference in lower esophageal sphincter (LES) pressure or pH. Small hiatal hernias ($< 3\text{cm}$) were eliminated in eight of 13 patients (62%) who had hernias at baseline. No serious complications arose. All patients reported transient pharyngeal irritation and moderate epigastric pain not requiring analgesics at the time of the procedure.

The second case series from Italy presented 12-month results of 20 patients enrolled over 22 months, from June 2006 to April 2008. All patients had PPI-dependent GERD for at least six months. Four patients with persistent GERD symptoms despite the use of standard PPI doses were scheduled for laparoscopic fundoplication at month six, and one patient was lost to follow-up. Seven patients (35%) had discontinued PPI therapy at 12 months. Eleven patients (55%) had an improved GERD-HRQL $> 50\%$ (median baseline GERD-HRQL = 40). There was no significant change from baseline in mean LES pressure and acid or non-acid reflux. Two additional patients (for a total of six of 20 patients, 30%) were scheduled for laparoscopic surgery after the 12-month follow-up for persistence of symptoms. Serious adverse events occurred in two patients with hematemesis on the first and eighth postoperative day. Both responded to in-hospital conservative management. Of note, in the four patients who underwent laparoscopic fundoplication at six months, fasteners were found partially extruded as if the stomach wall had disengaged from the H suture, which was still present on the esophageal side. Fasteners were easily removed.

The Plicator endoscopic suturing device was studied by Von Renteln et al (2009) in a 12-month industry-supported case series of 41 patients with PPI-dependent GERD. At 12 months, 24 of 41 patients (59%) had discontinued daily PPI therapy. Twenty-six of 41 patients (63%) had an improved GERD-HRQL $> 50\%$. GERD-HRQL scores improved from a median of 25 at baseline *off* PPI to 8 post-treatment, a statistically significant improvement ($p < 0.001$), and from a median of 11 at baseline *on* PPI to 8 post-treatment, a statistically significant improvement ($p = 0.015$). Acid exposure was not measured. All procedure-related adverse events occurred within the first post-procedure week.

Each of these case series is small with no comparator or control, and results that are statistically significant may not be clinically meaningful. The clinical trials database of the National Institutes of Health lists five active trials of the EsophyX device, including one sham-controlled and two active-controlled randomized trials. No active trials of the EndoCinch or Plicator devices were listed.

Transesophageal Radiofrequency

Aziz et al (2010) and investigators from the U.S. and Egypt conducted a 12-month randomized, double-blind, sham-controlled trial to assess radiofrequency (RF) energy applied to the gastroesophageal junction (i.e., the Stretta procedure). Thirty-six patients with antisecretory medication-dependent GERD for more than 6 months (mean = 7 years) were randomized to receive a single-session RF procedure, a double-session RF procedure for patients who had < 75% improvement of GERD-HRQL at four months, or a sham procedure. Each patient in the active treatment groups received 56 RF lesions per session. With the double-session group, the authors wished to examine whether 112 lesions created in two sessions several months apart were safer than 112 lesions created during a single session, which was the initial “dose” applied during development of the procedure and resulted in esophageal perforation in a few cases. Ten of 12 patients in the double-session group (83%) underwent both sessions.

At 12 months, two of 12 patients (17%) in the single-session group, six of 12 patients (50%) in the double-session group, and 0 of 12 patients in the sham group had discontinued antisecretory medication therapy. Within group comparisons showed statistically significant improvements in GERD-HRQL in all three treatment groups: In the single-session RF group, GERD-HRQL scores improved from a mean of 30 at baseline *off* meds to 14 post-treatment; in the double-session RF group, GERD-HRQL scores improved from 31 to 11; and in the sham group, GERD-HRQL scores improved from 30 to 25. Post-treatment values in the active treatment groups were significantly greater than the sham group ($p < 0.001$), but did not differ from each other ($p > 0.05$). Lower esophageal sphincter pressure increased in the active treatment groups to a statistically significant degree (from 12 mmHg to 16 mmHg in the single-session group, and from 12 mmHg to 20 mmHg in the double-session group; $p < 0.01$ for both groups) but not in the sham group (14 mmHg at baseline to 16 mmHg post-treatment, $p > 0.05$). The total time esophageal pH was less than 4.2 in a 24-hour period decreased to a statistically significant degree in the active treatment groups (from 9.4 minutes to 6.7 minutes in the single-session group ($p < 0.01$), and from 8.8 minutes to 5.2 minutes in the double-session group ($p < 0.01$) but not in the sham group (9.9 minutes at baseline to 8.2 minutes post-treatment ($p > 0.05$)). The clinical relevance of these changes is uncertain.

Transient post-procedure adverse events (retrosternal discomfort requiring oral analgesics, mild fever, nausea/vomiting, and dysphagia) were experienced by more patients in the active treatment groups than in the sham groups. Serious adverse events occurred in one patient in the single-session group who developed pneumonia and bilateral pleural effusion responsive to one week of inpatient antibiotics. Two patients who received double sessions of RF treatment developed prolonged gastroparesis. During 12 months of follow-up evaluation, one of these two patients showed mild improvement, whereas the other showed no improvement despite high doses of prokinetic medication. The authors speculate that “[w]orsening gastroparesis may be due to vagal injury during Stretta treatment, especially with a greater number of RF lesions.”

Injection of Polymer

No human studies of polymethylmethacrylate implantation for the treatment of GERD were identified for the 2010 policy update. The Web site of Carbon Medical Technologies, manufacturers of Durasphere®, a bulking agent approved for treatment of urinary and fecal

incontinence, states that Durasphere GR is an investigational device in the U.S. “intended to treat problems associated with GERD.” A search of the clinical trials database of the National Institutes of Health revealed no registered studies of Durasphere for GERD.

August 2011 Update EndoCinch™

Several papers have been published on laparoscopic Nissen fundoplication following failed transesophageal endoscopic therapies for GERD. Furnee et al (2010) reported prospectively collected data from 11 consecutive patients who underwent Nissen fundoplication after failure of EndoCinch™ gastroplication. The 11 patients were from a cohort of 50 (22%) who had been treated with EndoCinch™ from a randomized trial described above (20 randomized to EndoCinch™ and 30 controls who crossed over). Two patients had persistence of their primary symptoms after EndoCinch™ plication and the other nine experienced recurrence of symptoms after several months. Upper endoscopy showed disruption of between one and three of the gastroplications. Nissen fundoplication was performed without major complications at a medium of 23 months (range 7-33) after the EndoCinch™ procedure. After a median follow-up of 31 months (range, 6-61 months), nine patients (81.8%) reported their preoperative symptoms as resolved or improved. General quality of life improved from 33 to 79 on a visual analog scale. Three patients (27.3%) had daily complaints of troublesome dysphagia, a rate which compared unfavorably with the 3.6% rate reported after primary Nissen fundoplication. Another patient had troublesome chest pain. Acid exposure times were found to have increased slightly after EndoCinch™ and decreased after Nissen fundoplication.

In summary, comparative studies with EndoCinch™ have failed to show an improvement in acid exposure time when compared to sham and suggest inferior results when compared to laparoscopic surgery. There is a high rate of loss of intact sutures at one-year follow-up, and there are reports that laparoscopic fundoplication is common following failed EndoCinch™ procedure. A search of www.clinicaltrials.gov in June 2011 found no active trials with EndoCinch™.

EsophyX™

In 2011, Frazzoni et al. reported a small (n=20) prospective open-label study comparing the EsophyX™ procedure with laparoscopic Nissen fundoplication in PPI-resistant patients. Twenty-three of 142 patients who were assessed for persistent heartburn/regurgitation met the criteria for entering the study. Excluded were patients with Barrett’s esophagus, hiatal hernia, previous anti-reflux surgery, progressive systemic sclerosis, severe cardiac/pulmonary disease or pregnancy. Ten patients with PPI-resistant GERD chose to undergo EsophyX™ and ten chose laparoscopic fundoplication. There were no significant differences in baseline characteristics between the two groups. Ambulatory 24-hour impedance-pH monitoring was performed at baseline and three months after fundoplication. Distal and proximal refluxes were significantly reduced in the laparoscopic group (e.g., from a baseline of 73 to 25 at 3 months) but not in the endoscopic group (from 60 to 64). Esophageal acid exposure time was considered to be normal in 100% of cases after Nissen fundoplication versus 50% of cases after EsophyX™. Symptoms, based on a five-point Likert scale, remained in 0/10 laparoscopically treated patients and 6/10 patients who underwent EsophyX™. Although results from this small comparative study do not

support EsophyX™ in this select group of patients, randomized trials with a larger number of subjects and longer follow-up are needed to evaluate this procedure.

Velanovich et al (2010) reported on a series of 24 U.S. patients who underwent endoscopic fundoplication with EsophyX™. Patients considered candidates included those with symptomatic GERD that was responsive to PPIs, a small (<2 cm) hiatal hernia, objective pathologic evidence of GERD, and an absence of other esophageal motility disorders. Four patients had prior Nissen fundoplications with recurrent symptoms. Of the 24 EsophyX® patients, there was one major complication with a gastric mucosal tear. At an average seven-week follow-up (range, six to eight), 13 patients (54%) reported complete resolution of symptoms and six patients (25%) had persistent GERD-related symptoms. The median GERD-HRQL [Health-Related Quality of Life] improved from 25 to 5. In a letter to the editor in 2011, Velanovich reported that two of these patients subsequently had recurrence of GERD and failure of the EsophyX® fundoplication; the H-fasteners had pulled through the esophagus and were attached to the gastric fundus.

Bell and Freeman (2011) reported on an industry-funded series of 37 consecutive U.S. patients with PPI-resistant GERD and limited hiatal hernia (33% of patients), who underwent EsophyX® fundoplication. Five patients were reoperations for failed laparoscopic fundoplication. One patient had a complication requiring removal of the fundoplication and was not included in follow-up. At a median six-month follow-up (range, 3-14), no patient reported problems with dysphagia, bloating, or excess flatulence and 82% were not taking any PPIs. Symptoms were significantly improved compared to baseline on PPI's. Acid exposure was significantly improved and normalized in 61% of patients whose reflux characteristics on PPIs at baseline were elevated. Four patients had an increased acid exposure, two of whom underwent revision to laparoscopic Nissen fundoplication.

Barnes et al (2011) reported a retrospective study of 124 consecutive patients with PPI-resistant GERD who underwent EsophyX™ fundoplication at two community hospitals in the U.S. All patients had chronic GERD for a median of nine years (range 1-35) and were on daily double-dose of PPIs for a median of eight years (range 1-25); 97% reported ineffective symptom control on medical therapy. Out of 123 patients treated successfully, 110 (89%) gave consent for follow-up and completed GERD-specific questionnaires (baseline data was based on recall). Five patients underwent laparoscopic Nissen revision and were considered lost to follow-up, rather than treatment failures. Valves in two of these five patients were reported to have been disrupted due to retching and severe cough. At a median seven-month follow-up (range 5-17), typical and atypical symptom scores were normalized (no symptoms) in 75% to 80% of the remaining patients, and PPIs were discontinued by 93%. Endoscopy in 53 patients revealed Hill grade I tight valves in 89% of cases, reduced hiatal hernia in 33/34 (97%), and healed reflux esophagitis in 25/30 (83%). No patient complained of dysphagia or odynophagia. Based on global analysis, 72% of the patients were reported to be in remission, 20% improved symptomatically, and 8% had ongoing GERD. These case series are limited by the short follow-up, lack of control for placebo effects or reporting bias, and lack of objective measures of reflux.

In summary, the literature on the efficacy of Esophyx consists largely of case series. While these case series report improvements in outcomes following treatment with Esophyx, the lack of

control group makes the clinical meaning of these changes unclear. Randomized controlled trials with longer follow-up are needed to determine whether EsoPHYX improves outcomes compared to alternative treatments.

Gatekeeper Reflux Repair System

The available evidence for this device consists of one randomized, controlled trial by Fockens et al (2010). An industry-funded sham-controlled single-blind multicenter study randomized 118 patients into Gatekeeper (n=75) or sham (n=43) treatment. An additional 25 patients were treated as lead-ins during the initial training of investigators and included only in the safety analysis. The patients were implanted initially with four Gatekeeper prostheses. At three months, 44% of implanted patients received retreatment with up to four additional prostheses due to unsatisfactory symptom control. The primary safety end point was reduction in serious device- and procedure-related adverse device effects compared with a surgical procedure composite complication rate of 15%. Four serious adverse events were reported (two perforations, one pulmonary infiltrate related to a perforation, and one severe chest pain). The primary efficacy end point was reduction in heartburn symptoms using the GERD-HRQL (health-related quality of life) questionnaire. Planned interim analysis after 143 patients were enrolled found that heartburn symptoms and esophageal acid exposure had improved significantly in both the Gatekeeper and sham groups at six months, but there was no significant difference between the two groups. The study was terminated early due to a lack of efficacy.

December 2011 Update

A 2005 report of the Agency for Healthcare Research and Quality (AHRQ) on “Comparative Effectiveness of Management Strategies for Gastroesophageal Reflux Disease” found that more efficacy and safety data on new endoscopic approaches were needed. The comparative effectiveness review evaluated studies on the EndoCinch Suturing System, Stretta, Enteryx, and the NDO Plicator. A 2011 update of the AHRQ report excluded Enteryx and the NDO Plicator, since they were no longer available in the U.S., and added the EsoPHYX procedure (endoscopic fundoplication), which was commercialized after the 2005 review. The 2011 update reported the following:

- Like the 2005 Comparative Effectiveness Review (CER), the update did not identify any study that compared medical treatment with endoscopic therapy. The strength of evidence was rated insufficient.
- The review identified one small nonrandomized study that compared laparoscopic total fundoplication with EndoCinch. This study reported that laparoscopic total fundoplication was more effective than EndoCinch in improving GERD symptoms and decreasing acid exposure. The strength of evidence was rated insufficient.
- No study directly comparing endoscopic treatments was identified for the update. The strength of evidence was rated insufficient.
- Five cohort studies evaluated the effectiveness of EsoPHYX. The proportion of patients who were off proton pump inhibitors (PPIs) at the end of follow-up ranged from 47 to 71 percent. Significant improvement of quality of life as measured by the GERD-HRQL scale was reported by two of the five studies. The strength of evidence was rated insufficient.

- Common adverse events after endoscopic suturing included chest or abdominal pain (up to 24 percent), bleeding (up to 11 percent), dysphagia (up to 50 percent), and bloating (up to 19 percent). None of these quantitative estimates were reliable because of the lack of a standard definition and uniform system of reporting. The strength of evidence was rated low.

The AHRQ report concluded that for the three available endoscopic procedures (EndoCinch™, Stretta™, EsophyX™), effectiveness remains substantially uncertain for the long term management of GERD. While some clinical benefits were observed in patients who had these procedures, the studies were generally small, of variable quality, and of short duration. In addition, all of these procedures have been associated with complications, including dysphagia, infection/fever, and bloating. Higher quality studies are needed to determine the role and value of endoscopic procedures in the treatment of patients with GERD.

2012 Update

Plicator

A small randomized trial from Eastern Europe assigned 52 patients in a 2:1 ratio to transoral incisionless fundoplication (TIF) or to laparoscopic Nissen fundoplication. The first 18 patients randomized to TIF were treated with NDO Plicator™. After the company terminated production of the NDO Plicator™, the next 16 patients randomized to TIF were treated with Esophyx®. Results of this study are described below in the section on Esophyx®.

Esophyx®

The available literature on Esophyx® TIF consists of numerous case series, one small randomized controlled trial, one small non-randomized study with limited follow-up, and results from a multicenter registry.

Controlled trials. A small randomized trial assigned 52 patients in a 2:1 ratio to TIF (18 NDO Plicator™ and 16 Esophyx®) or to laparoscopic Nissen fundoplication. Patients were enrolled in the study if they had pathologic esophageal acid exposure confirmed by 24-hour pH measurements, responded at least partially to PPI therapy, showed a deteriorated gastroesophageal junction, and had a small hiatal hernia (<2 cm). At the 12-month follow-up, there were 26 patients (76%) in the TIF group and 14 patients (78%) in the Nissen fundoplication group. The GERD-HRQL improved to a similar extent in both groups. At 12 months, a similar percentage of patients in the TIF group (79%) and Nissen fundoplication group (73%) improved in the Hill grade by 50% or more, and the percentage of patients who had completely stopped PPI use was not significantly different (50% TIF vs. 71% Nissen). The hospital stay was significantly shorter following TIF group (2.9 days) compared to Nissen fundoplication (6.4 days).

Registry Data. In 2012, Bell and colleagues reported six-month follow-up from a prospective multicenter registry of patients with chronic GERD who received TIF using the EsophyX2 system with SerosaFuse fasteners. For the 100 consecutive patients who were treated in this community-based study, the median GERD symptom duration was nine years (range, 1-35 years), the median duration of PPI use was seven years (range, 1-20 years), and 92% of patients had incomplete symptom control despite maximal medical therapy. Fasteners were successfully

deployed in 89% of attempted deliveries, and a mean of 20 fasteners were used for fundoplication. Hiatal hernias of 2cm or less were completely reduced, while those greater than 2cm were partially reduced. The primary efficacy endpoint at six-months, the GERD-HRQL score, was normalized (score of 2 or less) in 73% of the 85 patients who had an abnormal GERD- HRQL score before the procedure. Median heartburn scores improved from 18 to 3, regurgitation scores improved from 15 to 0, and reflux symptom index score improved from 24 to 7. The percent of patients using PPIs decreased from 92% of patients before the procedure to 20% of patients after TIF, and an additional 9% of patients continued to use medications but no longer required daily PPI use. The authors noted that although the magnitude of typical symptom improvement was lower with TIF than is expected with traditional Nissen fundoplication, there was a very low incidence of side effects compared to traditional fundoplication.

Transesophageal Radiofrequency

Systematic Review and Meta-analyses. Perry et al. included 20 studies (2 RCTs and 18 case series) with a total of 1,441 patients in their meta-analysis. This review analyzed the within-subjects results following treatment only. The control groups of available clinical trials were not included for comparison.

Analysis of the nine studies (525 patients) that reported subjective heartburn scores showed a significant decrease from 3.55 to 1.19 at a mean of 24.1 months. Analysis of the nine studies (433 patients) that reported GERD-HRQL showed an improvement from 26.11 to 9.25 at a mean follow-up of 19.8 months. Analysis of the six studies (299 patients) that reported short-form (SF)-36 physical component scores showed an improvement from 36.45 to 46.12 at a mean follow-up of 9.5 months. For the 11 studies that measured esophageal pH, significant improvements were found in the Johnson-DeMeester score (from 44.37 to 28.53), the esophageal acid exposure time (from 10.29% to 6.51%), and lower esophageal sphincter pressure (from 16.54 to 20.24). This meta-analysis is limited by the inclusion of lower quality studies and by the analysis, which only examined within-subject differences and did not include between-subjects differences, as reported in the RCTs.

Arts and colleagues reported a double-blind randomized cross-over study of Stretta and sham treatment in 22 GERD patients. The initial sham treatment in 11 patients did not affect any of the outcome measures. Three months after the RF procedure, the symptom score was significantly improved (from 14.7 to 8.3), and gastro-esophageal junction compliance was significantly decreased (17.8 vs. 7.4 mL/mm Hg). The quality-of-life score for bodily pain improved from 49.5 to 24.0. No changes were observed in PPI use, esophageal acid exposure, or lower esophageal sphincter pressure after RF. The decrease in compliance of the gastro-esophageal junction was reversed by a smooth muscle relaxant, suggesting that the effect of RF on gastro-esophageal junction compliance was not due to fibrosis.

There is insufficient evidence at present to establish the safety and efficacy of these procedures, particularly in the long term. The studies presented are small, most are uncontrolled, and outcomes are of questionable clinical significance. Thus, they are unable to demonstrate improved net health outcomes for patients with GERD. High-quality data from large randomized controlled trials (RCTs) are needed to compare endoscopic procedures with the currently accepted treatments for GERD, namely drug therapy and laparoscopic fundoplication. Well-

designed RCTs should use standardized outcome measures to examine whether subjective improvement, such as discontinuation of medication therapy and GERD-HRQL scores, is supported by objective improvement, such as esophageal acid exposure. Until such studies demonstrate improved net health outcomes for patients with GERD, the policy statements are unchanged. These techniques are considered investigational.

2013 Update

Plicator™

A 2013 trial from Europe randomized 70 patients with GERD to endoscopic gastroplication with the Plicator or to laparoscopic fundoplication. Patients were followed for three months, and outcome measures included a variety of physiologic and symptom-based measures. On some outcomes, more effective relief of reflux-related symptoms was obtained after laparoscopic fundoplication, while on others the improvement was similar between groups. The Plicator was found to have a better side-effect profile, with a higher number of serious adverse events reported in the laparoscopic fundoplication group. There were 13 patients in the Plicator group that required additional anti-reflux procedures due to a lack of adequate improvement in symptoms.

Esophyx®

In 2013, Muls et al. published three-year follow-up results on 66 of 86 patients (77%) in the pivotal FDA trial who had been treated with the Esophyx® device. Twelve of the 66 (18%) underwent revisional procedures (two laparoscopic Nissen and ten TIF revisions) and were considered treatment failures. With a modified intent-to-treat analysis (n=66), a clinically significant reduction in GERD-HRQL (> 50% vs. pre- TIF) was observed in 65% of patients at three years. Of the 11 patients who underwent pH testing at the three-year follow-up visit, nine (82%) showed normalized pH.

Summary

There is insufficient evidence at present to establish the safety and efficacy of these procedures, particularly in the long term. Some of the unresolved issues include questions about the safety and durability of the device/treatment and lack of consistent improvement in objective measures (esophageal acid exposure) using these devices. Also, the rate of revisional procedures on longer follow-up may be high and needs to be further defined. A number of these devices (e.g., EndoCinch™, NDO Plicator™, Gatekeeper, Enteryx™) are no longer marketed in the U.S. or actively evaluated due to lack of efficacy and/or safety issues. For procedures that are still in development, high-quality data from large randomized controlled trials are needed to compare endoscopic procedures with both sham controls and with the currently accepted treatments for gastroesophageal reflux disease (GERD), namely drug therapy and laparoscopic fundoplication. Well-designed trials should use standardized outcome measures to examine whether subjective improvement, such as discontinuation of medication therapy and GERD-HRQL (Health-Related Quality of Life) scores, is supported by objective improvement, such as esophageal acid exposure. Until such studies demonstrate improved net health outcomes for patients with GERD, these techniques are considered investigational.

Practice Guidelines and Position Statements

Updated guidelines released by the American College of Gastroenterology in 2013 state that the usage of current endoscopic therapy or transoral incisionless fundoplication cannot be recommended as an alternative to medical or traditional surgical therapy. (Conditional recommendation, moderate level of evidence)

The Society of American Gastrointestinal Endoscopic Surgeons (SAGES) provided updated guidelines on endoluminal treatments for GERD in 2013. SAGES gave a weak recommendation based on low-quality evidence for the EsophyX procedure, stating that long-term data is not yet available and that further studies are required to define optimal techniques and most appropriate patient selection criteria, and to further evaluate device and technique safety. SAGES gave a strong recommendation based on high-quality evidence that Stretta is considered appropriate therapy for patients being treated for GERD who are 18 years of age or older, who have had symptoms of heartburn, regurgitation, or both for 6 months or more, who have been partially or completely responsive to anti-secretory pharmacologic therapy, and who have declined laparoscopic fundoplication.

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

The 2008 Medical Position Statement of the American Gastroenterological Association makes no recommendation for or against “the use of currently commercially available endoluminal antireflux procedures in the management of patients with an esophageal syndrome” based on insufficient evidence (Grade Insufficient).

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

NICE issued guidance in 2011 on endoluminal gastroplication for GERD, concluding that “The evidence on endoluminal gastroplication for gastro-oesophageal reflux disease raises no major safety concerns. Evidence from a number of randomized controlled trials (RCTs) shows a degree of efficacy in terms of reduced medication requirement in the short term, but changes in other efficacy outcomes are inconsistent and there is no good evidence of sustained improvement in

oesophageal pH measurements. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.”

2004 Guidance from NICE on regarding bulking agents for GERD found that “Current evidence on the safety and efficacy of endoscopic injection of bulking agents for gastro-oesophageal reflux disease does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research.”

Key Words:

Stretta procedure, gastroplication, Endo Cinch, treatment for gastroesophageal reflux disease, endoscopic gastroplication or gastroplasty, endoscopic gastroplasty, radiofrequency of the lower esophageal sphincter (LES), Enteryx™, PMMA, Plicator™, EsophyX™ System with SerosaFuse™, EndoGastric StomaphyX™, Durasphere®, Gatekeeper Reflux Repair System, NDO plicator™, Transoral Incisionless Fundoplication, TIF

Approved by Governing Bodies:

FDA approved—Bard endoscopic suturing system, March 20, 2001/ 510(k) approval.

FDA approved—Stretta, April 2001.

FDA approved—Autosuture Endoscopic Suturing Device, March 1994.

FDA approved—Endopath Endoscopic Tissue Fastening, March 1998.

FDA approved—Enteryx™ 2003 (FDA issued recall of Boston Scientific Enteryx Procedure Kits and Enteryx Injector single Packs October 14, 2005, Boston Scientific issued recall September 23, 2005)

FDA approved—NDO Surgical Plicator™, September 8, 2003 (510K)

FDA approved—EsophyX™ System with SerosaFuse™, September 14, 2007

FDA approved—EndoGastric StomaphyX™ Device and Accessories (endoluminal fastener and delivery system), March 9, 2007

Benefit Application:

ITS Home: No special benefit rules apply.

ITS Host: Not subject to bundling edits.

FEP contracts: Special benefit consideration may apply. Refer to member’s benefit plan. FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Current Coding:

There are no specific CPT codes describing the Stretta or endoscopic suturing procedures. The following CPT code should be used to report these services with the narrative of the specific service provided:

43201 Esophagoscopy, flexible, transoral; with directed submucosal injection(s), any substance—when used to administer one of the products listed in the policy.

- 43192 Esophagoscopy, rigid, transoral; with directed submucosal injection(s), any substance (Effective 01/01/2014)
- 43212 Esophagoscopy, flexible, transoral; with placement of endoscopic stent (includes pre- and post-dilation and guide wire passage, when performed) (Effective 01/01/2014)
- 43236 Esophagogastroduodenoscopy, flexible, transoral; with directed submucosal injections(s), any substance
- 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
- 43266 Esophagogastroduodenoscopy, flexible, transoral; with placement of endoscopic stent (includes pre- and post-dilation and guide wire passage, when performed) (Effective 01/01/2014)
- 43499 unlisted procedure of esophagus.

Previous Coding:

- 43219 Esophagoscopy, rigid or flexible; with insertion of plastic tube or stent (Deleted effective 01/01/2014)
- 0008T Upper gastrointestinal endoscopy including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; with suturing of the esophagogastric junction (**Code deleted effective January 1, 2007**)
- 0133T Upper gastrointestinal endoscopy, including esophagus, stomach, and either the duodenum and/or jejunum as appropriate, with injection of implant material into and along the muscle of the lower esophageal sphincter (e.g., for treatment of gastroesophageal reflux disease) (**Code deleted effective July 1, 2007**)
- S2215 Upper gastrointestinal endoscopy, including esophagus, stomach, and either the duodenum and/or jejunum as appropriate; with injection of implant material into and along the muscle of the lower esophageal sphincter for treatment of gastroesophageal reflux disease (**Code deleted effective January 1, 2006**)

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Policy History:

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Medical Policy Group, August 2011 (3): Updated Policy section, Key Points, Key Words & References

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Medical Policy Group, December 2011 (3): Updated Description, Key Points & References

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Medical Policy Group, December 2013 (3): Updated Description, Key Points and References; no change in policy statement

Medical Policy Group, December 2013 (3): 2014 Coding Update – added new codes 43192, 43212 and 43266 (effective 01/01/14); moved code 43219 to previous coding (deleted effective 01/01/14)

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.