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Endoscopic Radiofrequency Ablation or Cryoablation for Barrett's Esophagus

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Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Note: Treatment of Barrett's Esophagus with Photodynamic Therapy is addressed in medical policy 00234.

When Services Are Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider radiofrequency ablation for treatment of Barrett's esophagus with either high-grade dysplasia or low-grade dysplasia to be **eligible for coverage.**

When Services Are Considered Not Medically Necessary
Based on review of available data, the Company considers radiofrequency ablation for treatment of Barrett's esophagus in the absence of dysplasia to be **not medically necessary.****

When Services are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers cryoablation for Barrett's esophagus, with or without dysplasia to be **investigational.***

Background/Overview

Barrett's Esophagus and the Risk of Esophageal Carcinoma
The esophagus is normally lined by squamous epithelium. Barrett's esophagus is a condition in which the normal squamous epithelium is replaced by specialized columnar-type epithelium, known as intestinal metaplasia, in response to irritation and injury caused by gastroesophageal reflux disease (GERD). Barrett's esophagus occurs in the distal esophagus, may be of any length, may be focal or circumferential, and can be visualized by the endoscopist as being a different color than the background squamous mucosa. Confirmation of Barrett's esophagus requires biopsy of the columnar epithelium and microscopic identification of intestinal metaplasia.

Intestinal metaplasia is a precursor to esophageal adenocarcinoma, and esophageal adenocarcinoma is thought to result from a stepwise accumulation of genetic abnormalities in the specialized epithelium, which results in the phenotypic expression of histologic features of low-grade dysplasia (LGD) to high-grade dysplasia (HGD) to carcinoma. Two large epidemiologic studies published in 2011 reported the risk of

progression to cancer in patients with Barrett's esophagus. One study reported the rate of progression to cancer in more than 8,000 patients with a mean duration of follow-up of 7 years (range 1-20 years). The de novo progression to cancer from Barrett's esophagus at one year was 0.13%. The risk of progression was reported as 1.4% per year in patients with low-grade dysplasia and 0.17% per year in patients without dysplasia. This incidence translates into a risk of 10-11 times that of the general population. The other study identified over 11,000 patients with Barrett's esophagus and, after a median follow-up of 5.2 years, reported that the annual risk of esophageal adenocarcinoma was 0.12%. Detection of low-grade dysplasia on index endoscopy was associated with an incidence rate for adenocarcinoma of 5.1 cases per 1,000 person-years, and the incidence rate among patients without dysplasia was 1.0 case per 1,000 person-years. Risk estimates for patients with high-grade dysplasia were slightly higher.

The reported risk of progression to cancer in Barrett's esophagus in older studies was much higher, with an annual incidence of risk of 0.4-0.5% per year, with risk estimated at 30-40 times the general population. It is upon these higher risk estimates that current surveillance recommendations have been based.

Management of Barrett's Esophagus
The current management of Barrett's esophagus includes treatment of GERD and surveillance endoscopy to detect progression to HGD or adenocarcinoma. The finding of LGD typically warrants only follow-up and surveillance biopsies, whereas the finding of HGD or early-stage adenocarcinoma warrants mucosal ablation or resection (either endoscopic mucosal resection [EMR] or esophagectomy).

EMR, either focal or circumferential, provides a histologic specimen for examination and staging (unlike ablative techniques). A study provided long-term results for EMR in 100 consecutive patients with early Barrett's-associated adenocarcinoma (limited to the mucosa). The 5-year overall survival (OS) was 98% and metachronous lesions were observed in 11% of patients after a mean of 36.7 months. In a recent review by Pech and Ell, the authors state that circumferential EMR of the entire segment of Barrett's leads to a stricture rate of 50%, and recurrences occur at a rate of up to 11%.

Mucosal ablation techniques that are available consist of one of several thermal (multipolar electrocoagulation [MPEC], argon plasma coagulation [APC], heater probe, Nd:YAG laser, KTP-YAG laser, diode laser, argon laser, and cryoablation) or nonthermal (5-aminolevulinic acid [5-ALA] and photofrin photodynamic therapy [PDT]) techniques. PDT has been the only therapy shown in a randomized Phase III trial to significantly decrease the risk of carcinoma in Barrett's esophagus. Two hundred and eight patients with HGD were randomly assigned to PDT and omeprazole versus omeprazole alone. At 24 months' follow-up, 77% of patients treated with PDT had complete ablation of HGD versus 39% in the control group ($p<0.0001$) and occurrence of adenocarcinoma within a follow-up time of 3.6 years was 13% in the PDT group versus 20% in the control group ($p<0.006$) However, the use of PDT for Barrett's esophagus with HGD has recently decreased dramatically, due to the fact that is relatively expensive and associated with a high complication rate, including photosensitivity and esophageal stricture formation in up to 30% of patients treated with this method.

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The CryoSpray Ablation™‡ System (formerly the SprayGenix™‡ Cryo Ablation System, CSA Medical, Inc.) uses a low-pressure spray for spraying liquid nitrogen through an upper endoscope. Cryotherapy allows for treatment of uneven surfaces; however, disadvantages include the uneven application inherent in spraying the cryogen.

Treating HGD or mucosal cancer solely with ablative techniques risks undertreating the approximately 10% of patients who have undetected submucosal cancer, in whom esophagectomy would have been required.

The HALO System from BÂRRX Medical, Inc. (Sunnyvale, Calif.) uses radiofrequency (RF) energy and consists of 2 components: an energy generator and an ablation catheter. The generator provides rapid (i.e., less than 1 second) delivery of a predetermined amount of RF energy to the catheter. Both the HALO90 and HALO360 are inserted into the esophagus with an endoscope, using standard endoscopic techniques. The HALO90 catheter is plate-based and used for focal ablation of areas of Barrett's esophagus up to 3 cm. The HALO360 uses a balloon catheter that is sized to fit the individual esophagus and is inflated to allow for circumferential ablation.

Ablation with RF affects only the most superficial layer of the esophagus (the mucosa), leaving the underlying tissues unharmed. Efficacy measures of the procedure include eradication of intestinal metaplasia without leaving behind microscopic (or "buried") foci and post-ablation regrowth of the normal squamous epithelium. Reports of the efficacy of the HALO system in ablating Barrett's esophagus have been as high as 70% (comparable to alternative methods of ablation [e.g., APC and MPEC]), and even higher in some reports. The incidence of leaving behind "buried" foci of intestinal metaplasia has been reported to be 20–44% with APC and 7% with MPEC; reports using the HALO system have been 0%. Another potential advantage to the HALO system is that because it is automated, it eliminates operator-dependent error that may be seen with APC and MPEC.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
The HALO360 received U.S. FDA 510(k) clearance for marketing in 2005 and the HALO90 in 2006. The FDA-labeled indications are for use in coagulation of bleeding and non-bleeding sites in the gastrointestinal tract, and include the treatment of Barrett's esophagus. The CryoSpray Ablation System received FDA 510(k) marketing clearance in December 2007 for use as a "cryosurgical tool for destruction of unwanted tissue in the field of general surgery, specifically for endoscopic applications."

Rationale/Source

This policy was created in December 2008 and updated periodically with literature review. The most recent update covers the period of November 2010 through February 2012.

LITERATURE REVIEW

RFA versus surgical resection

Radiofrequency ablation (RFA) has been accepted as a less invasive alternative to surgical mucosal resection or esophagectomy, based on the results of randomized and non-randomized trials. Early single-

arm trials reported high rates of success in eradication of dysplastic and metaplastic tissue, with low rates of adverse effects. Semlitsch and colleagues reported a systematic review of this evidence for RFA of Barrett's esophagus based on a total of 9 observational studies and 429 patients. Inclusion criteria for the systematic review required that studies include patients with Barrett's esophagus and metaplasia or dysplasia for which RFA was the intervention (with or without endoscopic mucosal resection) and have a minimum follow-up period of 12 months. In 7 of the studies, the patients were treated with circumferential ablation followed by focal ablation, whereas 2 studies used only the circumferential method. The maximum number of ablations performed was reported in 7 studies and ranged from 2 to 5. Complete eradication of Barrett's esophagus with dysplasia and metaplasia was achieved in 71-100% and 46-100% of patients, respectively. Six cases of esophageal stenosis and one case of buried intestinal metaplasia were reported among all patients.

At least one randomized controlled trial (RCT) compared RFA to surgical mucosal resection. van Vilsteren and colleagues reported on the results of a multicenter, randomized trial which compared the safety of stepwise radical endoscopic resection (SRER) versus focal ER followed by RFA for complete eradication of Barrett's esophagus ≤5 cm containing high-grade dysplasia/early cancer. Patients in the SRER group underwent piecemeal ER of 50% of Barrett's esophagus followed by serial ER. Patients in the ER/RFA group underwent focal ER for visible lesions followed by serial RFA. Follow-up endoscopy with biopsies (4-quadrant/2 cm Barrett's esophagus) was performed at 6 and 12 months and then annually. Main outcome measures were: stenosis rate, complications, complete histological response for neoplasia (CR-neoplasia); and complete histological response for intestinal metaplasia (CR-IM). CR-neoplasia was achieved in 25/25 (100%) SRER and in 21/22 (96%) ER/RFA patients. CR-IM was achieved in 23 (92%) SRER and 21 (96%) ER/RFA patients. The stenosis rate was significantly higher in SRER (88%) versus ER/RFA (14%; $p<0.001$), resulting in more therapeutic sessions in SRER (6 vs. 3; $p<0.001$) due to dilations. After median follow-up of 24 months, one SRER patient had recurrence of early cancer, requiring endoscopic resection. This study confirmed that both techniques achieve comparably high rates of CR-IM and CR-neoplasia but that SRER was associated with a higher number of complications and therapeutic sessions.

Conclusions. RFA is a less-invasive alternative to surgical mucosal resection and/or esophagectomy. Available research supports that RFA results in similar efficacy for disease that has not extended into the submucosa, with fewer complications.

RFA versus surveillance alone in BE

One randomized multi-center, sham-controlled trial has been published that compares RFA to surveillance alone in Barrett's esophagus with dysplasia. This trial included patients with both HGD and LGD. 127 patients with dysplastic Barrett's esophagus were randomized in a 2:1 ratio to receive RFA or a sham procedure. The groups were randomly assigned according to the grade of dysplasia (low-grade [n=64] or high-grade [n=63]) and length of the Barrett's esophagus (<4 cm or 4-8 cm). Patients in the RFA group could receive up to 4 ablation sessions, performed at baseline and at 2, 4, and 9 months. Primary outcomes were the proportion of patients who had complete eradication of dysplasia at 12 months and the proportion of all patients who had complete eradication of intestinal metaplasia at 12 months. The proportion of patients who had progression of dysplasia was a secondary outcome, this included progression of LGD to

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HGD or cancer, and the progression of HGD to cancer. This trial was included in the 2010 TEC Assessment and was rated fair on formal quality assessment according to the U.S. Preventive Services Task Force system. The only obstacles to a good rating were missing details about random sequence generation and concealment of allocation.

Overall, complete eradication of intestinal metaplasia was 77.4% in the ablation group compared with 2.3% of the control group (p<0.001). Patients who did not receive RFA were more likely to have disease progression (16.3%) than those who received RFA (3.6%; p=0.03). Three serious adverse events occurred in the RFA group, including 1 episode of upper gastrointestinal hemorrhage, which was treated endoscopically, one overnight hospitalization for new-onset chest pain 8 days after RFA, and 1 night of hospitalization for an episode of chest discomfort and nausea immediately after RFA. No adverse events were observed in the control group. No esophageal perforations or procedure-related deaths occurred. Among patients in the RFA group, esophageal stricture developed in 5 patients (6%), all of whom successfully underwent dilated endoscopy.

In 2011, 2- and 3-year results of this trial were reported. Subjects were followed for a mean time of 3.05 years, with 106/127 (83%) patients included in the analysis. Outcomes included eradication of dysplasia or intestinal metaplasia after 2 and 3 years, durability of response, disease progression, and adverse events. After 2 years, 101 of 106 patients had complete eradication of all dysplasia (95%) and 99 of 106 had eradication of intestinal metaplasia (93%). Serious adverse events occurred in 4 of 119 subjects (3.4%). No perforations or procedure-related deaths occurred. The rate of esophageal stricture was 7.6%. The rate of esophageal adenocarcinoma was 1 per 181 patient-years (0.55%/patient-years); there was no cancer-related morbidity or mortality. The annual rate of any neoplastic progression was 1 per 73 patient-years (1.37%/ patient-years). The authors concluded that, for patients with dysplastic Barrett's esophagus, RFA is durable and associated with a low rate of disease progression for up to 3 years.

RFA for High-Grade Dysplasia. In patients diagnosed with Barrett's esophagus with high-grade dysplasia, risk of progression to cancer is relatively high and esophageal adenocarcinoma is associated with poor morbidity and a 5-year survival rate of 13% or less. Therefore, intervention with esophagectomy or radiofrequency ablation may be strongly indicated.

The Shaheen RCT reported that RFA was successful in eradicating HGD, with complete eradication achieved in 81% of the ablation group versus 19% in the control group (p<0.001) at 12 months. This trial also confirmed a high risk of progression to cancer in patients with HGD and established that this progression was significantly reduced in patients treated with RFA. Among 63 patients with HGD in that trial, 19% in the control group progressed to cancer versus 2.4% in the RFA group (p=0.04). This represented a nearly 90% relative risk reduction for progression to cancer (relative risk [RR]: 0.1, 95% CI: 0.01-1.0, p=0.04), and a number needed to treat of 6.0 to prevent one case of cancer over a one-year period.

Longer-term follow-up at 2-3 years reported that complete eradication of dysplasia was maintained in most participants with initial HGD. For 54 patients with HGD available for follow-up, all dysplasia was eradicated

in 50 of 54 (93%), and all intestinal metaplasia was eradicated in 48 of 54 (89%). After 3 years, dysplasia was eradicated in 55 of 56 of subjects (98%), and all intestinal metaplasia was eradicated in 51 of 56 (91%). More than 75% of high-grade patients remained free of intestinal metaplasia with a follow-up of longer than 3 years, with no additional therapy.

Conclusions. For patients with Barrett's esophagus (BE) and HGD, there is a relatively high risk of progression to cancer, and interventions to prevent progression are warranted. RFA results in high rates of complete eradication of dysplasia that is durable for at least 2 years. Evidence from one RCT reports that progression from HGD to cancer is reduced by approximately 90% following RFA, with rates of esophageal strictures of 6%.

Radiofrequency Ablation for Low-Grade Dysplasia. A 2010 TEC Assessment on the use of RFA plus surveillance versus surveillance alone in the treatment of nondysplastic and low-grade dysplastic Barrett's esophagus included the Shaheen et al. randomized trial and 4 single-arm studies. Additional studies were selected for inclusion if they were full-length, peer-reviewed articles in English, and studied Barrett's esophagus treated with RFA in a comparative study of any size, or a single-arm study of at least 40 patients. The conclusions of the Assessment were that among patients with nondysplastic or low-grade dysplastic Barrett's esophagus:

- The available evidence is insufficient to show that RFA plus surveillance achieves a better net health outcome than surveillance alone.
- The body of evidence on disease progression is too small and of too short duration to permit conclusions about the effects of RFA on this outcome.

In addition, the TEC Assessment discussed challenges in diagnostic differentiation between non-dysplastic Barrett's esophagus and Barrett's esophagus with low-grade dysplasia. Both sampling bias and interobserver variability have been shown to be problematic. Therefore, analysis of progression to carcinoma in Barrett's with intestinal metaplasia versus low-grade dysplasia is a challenge. Initial diagnosis of Barrett's esophagus can be a challenge with respect to histologic grading because inflammation and low-grade dysplasia can share similar histologic characteristics.

In the Shaheen RCT, there were 64 patients with LGD. At 12 months follow-up, the dysplasia was completely eradicated in 90.5% of those in the RFA group, compared with 22.7% of those in the control group ($p<0.001$). There were no patients in the LGD group that progressed to cancer over the initial 12 months. Progression to HGD was noted in 2/42 (5%) of patients in the RFA group, compared to 3/22 (14%) in the control group. The difference in rates of progression to HGD did not reach statistical significance (RR: 0.3, 95% CI: 0.1-1.9, $p=0.33$).

After 2 years, there were 52 subjects available who had initial LGD treated with RFA. Progression from LGD to HGD or cancer occurred in one patient, for an estimated rate of 2.0% per patient per year. In patients with initial LGD, all dysplasia was eradicated in 51 of 52 (98%), and all intestinal metaplasia was eradicated in 51 of 52 (98%).

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Further risk stratification of patients with LGD has been an active area of research, given the variable progression rates reported in the literature and the uncertain risk/benefit ratio of RFA when rates of progression are low. Attempts to define clinical and/or demographic factors, such as age, lesion size, or multifocal lesions, which predict progression, have been attempted. Although these factors have been found to be predictors of progression in some studies, it has not been possible to define an optimal cutoff for these factors that offers good discrimination between progressors and non-progressors.

Another line of research to risk-stratify patients with low-grade dysplasia has been to use multiple pathologists, including experts in gastrointestinal (GI) histopathology, to confirm the initial diagnosis of LGD. There is a high degree of intraobserver variability in pathologists' reading of LGD versus inflammatory changes, and this variability in pathology diagnosis may contribute to the variable rates of progression of LGD reported in the literature. Kerkhof et al. reported that in patients with an initial pathological diagnosis of LGD, review by an expert pathologists will result in downgrading the initial diagnosis to non-dysplasia in up to 50% of cases. Curvers et al. tested this hypothesis in 147 patients with BE who were given an initial diagnosis of LGD. All pathology slides were then read by 2 expert GI pathologists with extensive experience in BE, with disagreements among experts resolved by consensus. After review by expert pathologists, 85% of initial diagnoses of LGD were downgraded to non-dysplasia, leaving a total of only 22/147 patients (15%) with a confirmed diagnosis of LGD. All patients were followed for a mean of 5.1 years for progression to HGD or cancer. For patients with confirmed LGD, the rate of progression was 13.4%, compared with a rate of 0.5% for patients who had been downgraded to non-dysplasia.

Conclusions. The risk of progression from LGD to cancer is not well-defined, with highly variable rates reported in the published literature. Evidence from randomized and non-randomized studies establishes that RFA can achieve complete eradication of dysplasia in patients with LGD that is durable for at least 2 years. However, in the single RCT there were only a limited number of patients that progressed from LGD to HGD, and there was not a significant reduction in progression for patients treated with RFA. As a result the risk/benefit ratio of treating all patients with an initial diagnosis of LGD is less certain.

Radiofrequency Ablation for Non-Dysplastic BE. There are no RCTs that evaluate treatment of non-dysplastic BE with RFA. The evidence on this question consists of single arm trials that report outcomes of RFA. This evidence can provide useful data on the success in eradicating dysplasia, but cannot provide high-quality evidence on the comparative efficacy of RFA versus surveillance alone. Progression to cancer in non-dysplastic BE is lower than that for LGD or HGD, with rates in the literature ranging from 0.05-0.5%.

Fleischer and colleagues reported the 5-year follow-up of a single-arm study of patients with non-dysplastic Barrett's esophagus treated with RFA. The original study included 70 patients who underwent circumferential RFA and complete-response-intestinal metaplasia (CR-IM); defined as complete eradication of nondysplastic Barrett's esophagus, CR-IM was seen in 70% of patients at 1-year follow-up; patients with persistent Barrett's esophagus underwent focal RFA. At the 2.5 year follow-up, CR-IM was found in 60 of 61 patients (98%). At 5 year follow-up, 4-quadrant biopsies were obtained from every 1 cm of the original extent of Barrett's esophagus, and the authors reported the proportion of patients demonstrating CR-IM. If nondysplastic Barrett's esophagus was identified at the 5-year follow-up, focal RFA was performed 1 month

later and re-biopsy 2 months after to assess histologic response. Primary outcomes were the proportion of patients demonstrating CR-IM at 5-year biopsy or after single session focal RFA. For the 5-year follow-up, there were 60 eligible patients, 50 (83%) of whom were willing to participate. Forty-six of 50 patients (92%) showed CR-IM at the 5-year biopsy visit. The four patients found to have Barrett's esophagus at 5 years underwent a single session of RFA 1 month after biopsy, and all were found to have CR-IM at subsequent re-biopsy 2 months after RFA. No strictures were noted. The authors concluded that this first report of 5-year CR-IM outcomes lends support to the safety, efficacy, cost-utility, and reduction in neoplastic progression in treating non-dysplastic Barrett's esophagus with RFA.

Conclusions. Non-dysplastic BE has a relatively low rate of progression to cancer. Although available research reports that non-dysplastic metaplasia can be eradicated by RFA, the risk/benefit ratio and the net effect on health outcomes is uncertain. It is possible that the risk of RFA exceeds the benefit in this population, owing to the low underlying rates of progression and the reported rates of esophageal strictures following RFA.

Cryoablation of BE
Published efficacy data for cryoablation in Barrett's esophagus are limited. Johnston and colleagues conducted a prospective, single-center pilot study in 11 men with Barrett's esophagus and degrees of dysplasia ranging from none to multifocal HGD. The mean length of Barrett's was 4.6 cm (range: 1–8 cm). After 6 month follow-up, complete histologic eradication of Barrett's esophagus was achieved in 7 of the 9 patients (78%), completing the protocol.

An open-label, single-center, prospective, nonrandomized cohort study assessed the safety of cryoablation as a treatment option for Barrett's esophagus with HGD or early cancer (intramucosal carcinoma). Thirty patients who were either deemed high-risk surgical candidates or who refused esophagectomy underwent cryoablation. Twenty-seven patients (90%) had downgrading of pathology stage after treatment. After a median follow-up period of 12 months, elimination of cancer or downgrading of HGD was 68% for HGD and 80% for intramucosal cancer.

Greenwald and colleagues reported the safety, tolerability, and efficacy of low-pressure liquid nitrogen spray cryotherapy in 77 patients from multiple institutions who underwent a total of 377 procedures for Barrett's esophagus with HGD (58.4%), intramucosal carcinoma (16.9%), invasive carcinoma (13%), Barrett's esophagus without dysplasia (9.1%), and severe squamous dysplasia (2.6%). The main outcome measurement was the incidence of serious adverse events and side effects from treatments. No side effects were reported by 28.6% of patients. The most common side effects were chest pain (18%), dysphagia (13%), odynophagia (12.1%), and sore throat (9.6%). Esophageal stricture occurred in 3 patients, all of which were successfully treated with dilation, and gastric perforation occurred in one patient. Complete response for HGD, all dysplasia, intestinal metaplasia, and cancer were assessed in patients completing therapy during the study period and having at least 1 follow-up endoscopy with biopsy for assessment of histologic regression of the underlying lesion (n=23). For patients with HGD (n=17), complete response (CR) of the HGD, any dysplasia, and intestinal metaplasia was 94%, 88% and 53%, respectively. For patients with intramucosal carcinoma (n=4), 100% had complete response of the cancer,

HGD, and any dysplasia, and 75% had complete response of intestinal metaplasia. For the patients with invasive cancer (n=3), 100% had complete response of the cancer, HGD, and any dysplasia, and 67% of intestinal metaplasia.

Shaheen and colleagues reported a multicenter, retrospective cohort study of 98 consecutive patients with Barrett's esophagus with HGD treated with spray cryotherapy to assess the safety and efficacy. A total of 333 treatments (mean 3.4 per patient) were performed, and cryotherapy was performed with the intent to eradicate all Barrett's esophagus. Sixty patients completed all planned cryotherapy treatments and were assessed for efficacy with follow-up endoscopy sessions with 4 quadrant biopsies performed every 1-2 cm. Fifty-eight patients (97%) had complete eradication of HGD, 52 (87%) had complete eradication of all dysplasia with persistent nondysplastic intestinal metaplasia, and 34 (57%) had complete eradication of all intestinal metaplasia. There were no esophageal perforations, and esophageal stricture occurred in 3 patients. The authors noted the limitations of the study as it was nonrandomized, retrospective without a control group, lacked centralized pathology, used surrogate outcomes for decreased cancer risk, and had a short follow-up (10.5 months).

Conclusions. There is limited evidence on the use of cryoablation for treatment of BE and no controlled trials. The evidence from uncontrolled studies report high rates of success in eradicating dysplasia, with low rates of complications. These data are not sufficient to determine the comparative efficacy of cryoablation compared to RFA.

Clinical Input Received Through Physician Specialty Societies and Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted. In response to requests in 2009, input was received related to use of radiofrequency ablation (cryoablation was not included in the request) from 3 academic medical centers and from the American Gastroenterological Association (AGA). All reviewers and the AGA agreed that RFA should be considered medically necessary for the treatment of Barrett's with HGD. The reviewers were split for the use of RFA for LGD, with 9 in favor of it being medically necessary and 4 considering it investigational.

Clinical input was again requested when this policy was under review in 2012, with focus on the treatment of LGD. At this time, input was received from reviewers at 6 academic medical centers and from the American Gastroenterological Association. For the treatment of LGD, input was mixed, with 2 reviewers stating that RFA for LGD should be investigational, 3 indicating that it should be medically necessary, and 2 indicating that it was a split decision. There was general consensus among reviewers that there are subpopulations of patients with LGD who have higher risk and should therefore be treated. Reviewers mentioned the confirmation of LGD diagnosis by multiple pathologists, and/or the application of clinical high-risk factors such as lesion length, as factors that were useful to define higher-risk populations that warrant treatment.

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Summary
RFA of HGD in Barrett's esophagus has been shown to be at least as effective in eradicating high-grade dysplasia as other ablative techniques with a lower progression rate to cancer and may be considered as an alternative to esophagectomy. Therefore, RFA may be considered medically necessary for patients with BE and HGD.

For patients with LGD, the benefit of RFA is less certain, as the rate of progression to cancer is variable in the literature. There are no high-quality trials that treat patients with an initial diagnosis of LGD and report improved outcomes. However, based on the available evidence, specialty society guidelines, and the results of clinical vetting, it is likely that the benefit of treatment outweighs the risk. As a result, RFA of LGD may be considered medically necessary.

For patients with non-dysplastic BE, it cannot be concluded that the benefit of RFA outweighs the risk, and therefore RFA is considered not medically necessary for this population. Data for the efficacy of cryoablation of BE with or without dysplasia are limited. The studies consist of small numbers of patients with short-term follow-up, and therefore cryoablation of BE is considered investigational.

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Coding

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Endoscopic Radiofrequency Ablation or Cryoablation for Barrett's Esophagus

Policy # 00261
Original Effective Date: 06/16/2010
Current Effective Date: 01/15/2014
Returned to Active Status: 01/15/2014

Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	43257, 43229, 43270 (Codes 43228, 43258 deleted as of 01/01/2014)
HCPCS	No code
ICD-9 Diagnosis	211.0, 530.85
ICD-9 Procedure	42.33

Policy History

Original Effective Date: 06/16/2010
Current Effective Date: 01/15/2014

06/03/2010	Medical Policy Committee approval
06/16/2010	Medical Policy Implementation Committee approval. New policy.
05/05/2011	Medical Policy Committee approval
05/18/2011	Medical Policy Implementation Committee approval. No change to coverage.
04/12/2012	Medical Policy Committee review
04/25/2012	Medical Policy Implementation Committee approval. Radiofrequency ablation for treatment of Barrett's esophagus with low-grade dysplasia was changed from investigational to eligible for coverage when the initial diagnosis of low-grade dysplasia is confirmed by a second pathologist who is an expert in GI pathology. Added that treatment of Barrett's esophagus with low-grade dysplasia in any other situation is investigational.
03/04/2013	Coding revised
04/04/2013	Medical Policy Committee review
04/24/2013	Medical Policy Implementation Committee approval. No change to coverage.
06/25/2013	Medical Policy Implementation Committee approval. Retired medical policy.
01/09/2014	Medical Policy Committee review
01/15/2014	Medical Policy Implementation Committee approval. "Based on review of available data, the Company considers radiofrequency ablation for treatment of Barrett's esophagus in the absence of dysplasia" was changed from investigational to not medically necessary. Dropped the requirement of a second pathologist from coverage section. Brought back from retired status.

Next Scheduled Review Date: 01/2015

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means

of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:

1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
2. credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
3. reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. in accordance with nationally accepted standards of medical practice;
B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and 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.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.