Policy Statement

Peroral endoscopic myotomy is considered investigational as a treatment for esophageal achalasia.

Policy Guidelines

There are no specific CPT codes for this procedure. The following CPT code would likely be reported:
- **43499**: Unlisted procedure, esophagus

Description

Esophageal achalasia is characterized by reduced numbers of neurons in the esophageal myenteric plexuses and reduced peristaltic activity, making it difficult for patients to swallow food and possibly leading to complications such as regurgitation, coughing, choking, aspiration pneumonia, esophagitis, ulceration, and weight loss. Peroral endoscopic myotomy (POEM) is a novel endoscopic procedure that uses the oral cavity as a natural orifice entry point to perform myotomy of the lower esophageal sphincter. This procedure is intended to reduce the total number of incisions needed and thus the overall invasiveness of surgery.

Related Policies

- N/A

Benefit Application

Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates [e.g., Federal Employee Program (FEP)] prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

POEM uses available laparoscopic instrumentation and, as a surgical procedure, is not subject to regulation by the U.S. Food and Drug Administration.

Rationale

Background

**Esophageal Achalasia**

Esophageal achalasia is characterized by reduced numbers of neurons in the esophageal myenteric plexuses and reduced peristaltic activity, making it difficult for patients to swallow food and possibly leading to complications such as regurgitation, coughing, choking, aspiration...
pneumonia, esophagitis, ulceration, and weight loss. The estimated U.S. prevalence of achalasia is 10 cases per 100,000, and the estimated incidence is 0.6 cases per 100,000 per year.¹

**Treatment**

Treatment options for achalasia have included pharmacotherapy such as injections with botulinum toxin, pneumatic dilation, and laparoscopic Heller myotomy.¹² Although the last 2 are considered the mainstay of treatment because of higher success rates and relatively long-term efficacy compared with pharmacotherapy and botulinum toxin injections; both are associated with a perforation risk of about 1%. Laparoscopic Heller myotomy is the most invasive of the procedures, requiring laparoscopy and surgical dissection of the esophagogastric junction.²

One-year response rates of 86% and major mucosal tear rates requiring subsequent intervention of 0.6% have been reported.³

Peroral endoscopic myotomy (POEM) is a novel endoscopic procedure developed in Japan.²⁴ POEM is performed with the patient under general anesthesia.⁵ After tunneling an endoscope down the esophagus toward the esophageal-gastric junction, a surgeon performs the myotomy by cutting only the inner, circular lower esophageal sphincter muscles through a submucosal tunnel created in the proximal esophageal mucosa. POEM differs from laparoscopic surgery, which involves complete division of both circular and longitudinal lower esophageal sphincter muscle layers. Cutting the dysfunctional muscle fibers that prevent the lower esophageal sphincter from opening allows food to enter the stomach more easily.²⁵

Note that the acronym POEM in this review refers to peroral endoscopic myotomy. POEMS syndrome, which has a similar acronym, is discussed in Blue Shield of California Medical Policy: Hematopoietic Cell Transplantation for Plasma Cell Dyscrasias, Including Multiple Myeloma and POEMS Syndrome

**Literature Review**

Assessment of efficacy for therapeutic intervention involves a determination of whether an intervention improves health outcomes. The optimal study design for this purpose is a randomized controlled trial that includes clinically relevant measures of health outcomes. Intermediate outcome measures, also known as surrogate outcome measures, may also be adequate if there is an established link between the intermediate outcome and true health outcomes. Nonrandomized comparative studies and uncontrolled studies can sometimes provide useful information on health outcomes but are prone to biases such as noncomparability of treatment groups, placebo effect, and variable natural history of the condition.

Literature included in this review on the efficacy of peroral endoscopic myotomy (POEM) is comprised of systematic reviews, nonrandomized comparative studies, and several case series studies. No randomized controlled trials comparing POEM with other treatment options have been found. The following summarizes the systematic reviews, nonrandomized studies, and select larger (≥50 patients) case series on this procedure.

**Peroral Endoscopic Myotomy**

**Systematic Reviews**

Several systematic reviews have evaluated outcomes of POEM. Three reviews have summarized outcomes of case series studies.⁶⁻⁸ The systematic review by Akintoye et al (2016) evaluated outcomes for 2373 patients from 36 studies.⁶ Clinical success rates were achieved in 98% of patients (95% confidence interval, 97% to 100%) and mean Eckardt scores decreased from baseline at 1, 6, and 12 months. (The Eckardt score grades 4 major symptoms of achalasia [dysphagia, regurgitation, retrosternal pain, weight loss] each on a 0 [none] to 3 [severe] scale, for a maximum score of 12; total scores of ≥4 represent treatment failure.⁹) The systematic review by Crespin et al (2017) evaluated outcomes for 1299 patients from 19 studies.⁷ Improvements in Eckardt scores were statistically significant in all studies. The most frequently reported complications were mucosal perforation, pneumothorax, pneumoperitoneum, and
subcutaneous emphysema. The systematic review by Patel et al (2016) evaluated outcomes for 1122 patients from 22 studies. Eckardt scores dropped from 6.8 at baseline to 1.2 postoperatively. There were improvements in lower esophageal sphincter (LES) pressure and symptoms.

Two systematic reviews only selected studies comparing POEM with an alternative surgical treatment. We only report results from the systematic review by Marano et al (2016) because it included the period covered in the other review and assessed more patients and studies. Marano evaluated outcomes for 486 patients (196 receiving POEM, 290 receiving laparoscopic Heller myotomy [LHM]) from 11 studies. None were randomized. Reviewers rated all studies as having a moderate risk of bias. No information on differences in disease severity between treatment groups was provided. There were no significant differences in the reduction of Eckardt scores, postoperative pain scores, or requirements for analgesics between procedures. Hospital length of stay was shorter for POEM.

**Section Summary: Systematic Reviews**

Conclusions on comparative efficacy cannot be determined from these systematic reviews because reviews of case series do not assess comparator treatments. The systematic reviews evaluating comparative studies only assessed nonrandomized studies and did not appear to have taken into account differences in patient characteristics.

**Nonrandomized Comparative Studies**

In a nonrandomized trial with historical controls, Hungness et al (2013) reported on perioperative outcomes in patients with achalasia treated with POEM (n=18) or LHM (n=55) at a single U.S. center. Surgical times were shorter for POEM (113 minutes) than for LHM (125 minutes; p<0.05). Additionally, estimated blood loss was lower in patients treated with POEM (≤10 mL in all POEM cases vs 50 mL for LHM, p<0.001). Myotomy lengths, complication rates, and length of stay were also similar between groups. Pain scores were similar post anesthesia and postoperatively on the first day, but were higher at 2 hours for POEM patients (3.5 vs 2.0, p=0.03). Narcotic use was similar between groups, although fewer patients treated with POEM received ketorolac, a nonsteroidal anti-inflammatory. POEM patients' median Eckardt scores decreased (1 postoperative vs 7 preoperative, p<0.001), and 16 (89%) patients had treatment success (score ≤3) at a median of 6 months follow-up.

In a retrospective study of a prospective database at Oregon Health & Sciences University, Bhayani et al (2014) compared outcomes in 37 patients who underwent POEM, and 64 patients who underwent LHM for achalasia. Full-thickness esophageal injury occurred in 4 POEM patients, and 8 esophageal and 3 gastric perforations occurred in LHM patients. Mean hospitalization was 1.1 days in the POEM group and 2.2 days in the LHM group (p<0.001). Eckardt scores were statistically lower postoperatively in the POEM group than in the LHM group (p<0.001), but at 6 months (64% of patients assessed), Eckardt scores did not differ statistically between groups (p=0.1). Postoperative decreases in LES pressures were similar between groups. At 6 months, resting LES pressure was higher in the POEM group (16 mm Hg) than in the LHM group (7 mm Hg; p=0.006). (LES pressure >15 mm Hg predicts recurrent dysphagia.)

In a retrospective study of patients with type III achalasia, Kumbhari et al (2015) compared outcomes for 49 patients who underwent POEM and 25 patients who underwent LHM. Defining clinical response as a reduction in Eckardt score of no more than 1, clinical response was more frequent in the POEM group (98.0%) than the LHM group (80.8%; p=0.01). However, LHM patients had more severe disease by several different measures. On multivariable analysis, there was no statistically significant difference in the odds of failure between procedures, although the point estimate of the odds favored POEM (odds ratio, 11.32; p=0.06). Procedure times were shorter with POEM. There was no difference in length of stay. The overall rate of adverse events was lower in the POEM group (6% vs 27%, p=0.01).

Ujiki et al (2013) compared outcomes for 18 patients undergoing POEM with 21 patients undergoing LHM. Postoperative Eckardt scores were similar (POEM 0.7 vs LHM 1.0). Several
outcomes related to recovery from surgery favored POEM (postoperative pain, analgesic use, return to activities of daily living).

Sanaka et al (2016) compared outcomes in their own institution for 36 patients undergoing POEM, 142 undergoing LHM, and 36 undergoing pneumatic dilation. At baseline, patients undergoing the 3 procedures had different characteristics. POEM patients were older, had higher body mass index, and had more prior treatments. After treatment, patients undergoing all 3 procedures had significant improvements as measured by high-resolution esophageal manometry and timed barium esophagram. Eckhardt symptom scores were only available for POEM patients. Long-term outcomes were not reported.

Wang et al (2016) retrospectively reviewed outcomes for POEM (n=21) and pneumatic dilation (n=10) in patients ages 65 years and older. All were treated successfully, with decreases in Eckhardt scores. At a mean follow-up of 21.8 months for POEM and 35 months for pneumatic dilation patients, 1 POEM case failed, and 2 pneumatic dilation procedures failed.

Section Summary: Nonrandomized Comparative Studies
The nonrandomized studies comparing POEM with other procedures are retrospective and involved patients who may not be comparable. Although outcomes were generally similar between POEM and the comparator treatments (LHM, pneumatic dilation), potential confounding and selection bias make outcome comparisons uncertain. The comparative studies did not report long-term outcomes.

Case Series
We now discuss a cross-section of the series evaluating the use of POEM. Inoue et al (2015) reported outcomes on 500 consecutive patients at a Japanese institution. Outcomes were available for a variable proportion of patients at different intervals after the procedure: 302 (60.4%) at 2 months, 102 (27.6%) of 370 at 1 to 2 years, and 61 (58.1%) of 105 at more than 3 years. The median Eckardt score at all time points was 1. LES pressure ranged from 13.4 to 11.7 mm Hg. Between 16.8% and 21.3% of subjects reported symptoms of gastroesophageal reflux disease. The overall complication rate was 3.2%.

Ramchandani et al (2016) reported outcomes on 200 consecutive patients at an institution in India. Outcomes at 1 year were available for 102 patients. Clinical success, defined as an Eckardt score of 3 or less, was achieved in 92% on a per-protocol analysis and 83% on intention-to-treat analysis, which included additional patients with technical failure and patients lost to follow-up. The mean Eckardt score was 1.18 after POEM.

In a prospective case series, von Renteln et al (2013) reported on 70 patients who underwent POEM at 5 centers in Europe and North America. Mean follow-up was 10 months (range, 3-12 months). Follow-up evaluations at 6 months and 1 year showed sustained treatment success of 89% and 82%, respectively. Mean pretreatment Eckardt scores were 6.9 compared with 1.3 at 6 months and 1.7 at 1 year (p<0.001 for both comparisons vs pretreatment score). In multivariate analysis, neither age, previous treatment (botulinum toxin injection, dilatation), myotomy length, preprocedure LES pressure, pretreatment Eckardt score, sex, procedure duration, nor full-thickness dissection during POEM were significant predictors of treatment failure at 1 year. At 3 months after POEM, esophagitis was observed in 42% of cases. However, the severity of esophagitis was minor (grade A or B), and all patients could be managed adequately with proton pump inhibitor therapy. At 3 months, 22% of patients required occasional and 12% required daily proton pump inhibitor therapy. The 1-year follow-up evaluation showed overall rates of gastroesophageal reflux disease of 37% and proton pump inhibitor use of 29%. Other complication rates of POEM ranged from 1% to 4%.

Teitelbaum et al (2014) also evaluated 1-year outcomes after POEM. Forty-one patients treated at an academic medical center and more than 1 year post-POEM were included. Most patients (37 [90%]) had no previous endoscopic treatment (botulinum toxin injection or pneumatic
Dilation). Ninety-two percent of 39 patients available for symptom assessment had treatment success (Eckardt score <4). In 21 patients evaluated, mean LES pressure was 11 mm Hg.

Ling et al (2014) reported quality of life outcomes in 2 patient cohorts (probably overlapping) who underwent POEM for achalasia at a single center in China. Quality of life was assessed at pretreatment and at 1-year follow-up using the 36-Item Short-Form Health Survey; Physical Component Summary and Mental Component Summary raw scores were transformed to a 0 (poor health) to 100 (good health) scale. In a group of 21 patients who had failed previous pneumatic dilation, mean Physical Component Summary scores improved from 30 to 65, and mean Mental Component Summary scores improved from 43 to 67 (p<0.001 for both comparisons). Incidences of intraoperative subcutaneous emphysema and pneumothorax were 14% and 5%, respectively; postoperative esophagitis developed in 19%. In 87 previously untreated patients, mean Physical Component Summary scores improved from 33 to 69 (p<0.001), and mean Mental Component Summary scores improved from 44 to 67 (p=0.003). Incidence rates of intraoperative subcutaneous emphysema and pneumothorax were 12% and 1% respectively; postoperative esophagitis developed in 6%.

A study by Ren et al (2012) highlighted POEM-specific complications. In this series of 119 cases, 23% of patients developed subcutaneous emphysema intraoperatively and another 56% postoperatively. Three of these patients required subcutaneous needle decompression. Additionally, 3% patients developed a pneumothorax intraoperatively and another 25% postoperatively. Postoperatively, the incidence of thoracic effusion was 49%; incidence of mild inflammation or segmental atelectasis of the lungs was 50%. All complications were resolved with conservative treatment.

At least 2 small case series (both 2013) have evaluated the efficacy and feasibility of POEM for patients with failed LHM/achalasia recurrence; success rates have been reported in over 90% of cases up to 10 months after rescue POEM. Studies also have compared different POEM techniques; comparable outcomes have been reported between patients undergoing full-thickness and circular myotomy.

**Section Summary: Case Series**
Case series have shown improvements in symptoms of achalasia after POEM. Such studies do not permit comparison with other established treatments.

**Summary of Evidence**
For individuals who have achalasia who receive POEM, the evidence includes systematic reviews, nonrandomized comparative studies, and case series. Relevant outcomes are symptoms, functional outcomes, health status measures, resource utilization, and treatment-related morbidity. The comparative studies have primarily reported similar outcomes with POEM and with Heller myotomy for symptom relief, as assessed by the Eckardt score. Some studies have shown shorter length of stay and less postoperative pain with POEM. However, potential imbalances in patient characteristics in these nonrandomized studies might have biased the treatment comparisons. In the case series, treatment success at short follow-up periods was reported for a high proportion of patients treated with POEM. However, the incidence of adverse events was relatively high, with POEM-specific complications, including subcutaneous emphysema, pneumothorax, and thoracic effusion, reported across studies. Additionally, a substantial proportion of patients undergoing POEM developed esophagitis and required treatment. Case series do not permit conclusions about the efficacy of POEM relative to established treatment, and long-term outcomes of the procedure are not well described in the literature. The evidence is insufficient to determine the effects of the technology on health outcomes.
Supplemental Information
Practice Guidelines and Position Statements

American Society of Gastrointestinal and Endoscopic Surgeons
In 2014, the American Society of Gastrointestinal and Endoscopic Surgeons issued evidence-based, consensus guidelines on the use of endoscopy in the evaluation and management of dysphagia, including esophageal achalasia28 The Society recommended that: “... Endoscopic and surgical treatment options for achalasia should be discussed with the patient. In patients who opt for endoscopic management and are good surgical candidates, pneumatic dilation with large-caliber balloon dilators for the endoscopic treatment of achalasia was recommended... Long-term data and randomized trials comparing peroral endoscopic myotomy to conventional modalities of management are necessary before it can be adopted into clinical practice, but the procedure is becoming more widely used in expert centers.”

American College of Gastroenterology
In 2013, the American College of Gastroenterology issued clinical guidelines on the diagnosis and management of achalasia.29 Peroral endoscopic myotomy was discussed as an emerging therapy and stated to have promise as an alternative to the laparoscopic approach. The guidelines further stated that randomized prospective comparison trials are needed, and the procedure should be performed in the context of clinical trials.

Society of American Gastrointestinal and Endoscopic Surgeons
In 2012, the Society of American Gastrointestinal and Endoscopic Surgeons issued evidence-based, consensus guidelines on the surgical management of esophageal achalasia. The guidelines stated that the peroral endoscopic myotomy technique “is in its infancy and further experience is needed before providing recommendations.”30

U.S. Preventive Services Task Force Recommendations
Not applicable.

Medicare National Coverage
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 1.

Table 1. Summary of Key Trials

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<td>NCT01793922</td>
<td>A Prospective Randomized Multi-center Study Comparing Endoscopic Pneumodilation and Per Oral Endoscopic Myotomy (POEM) as Treatment of Idiopathic Achalasia</td>
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NCT: National Clinical Trial.

References


**Documentation for Clinical Review**

- No records required

**Coding**

This Policy relates only to the services or supplies described herein. Benefits may vary according to product design; therefore, contact language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement.

**IE**

The following services may be considered investigational.

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Definitions of Decision Determinations

**Medically Necessary:** A treatment, procedure, or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

**Investigational/Experimental:** A treatment, procedure, or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California/Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a split evaluation, where a treatment, procedure, or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

**Prior Authorization Requirements (as applicable to your plan)**

Within five days before the actual date of service, the provider must confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.