Clinical Review Criteria
Peroral Endoscopic Myotomy (POEM) for Esophageal Achalasia

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Criteria
For Medicare Members

<table>
<thead>
<tr>
<th>Source</th>
<th>Policy</th>
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<tbody>
<tr>
<td>CMS Coverage Manuals</td>
<td>None</td>
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<tr>
<td>National Coverage Determinations (NCD)</td>
<td>None</td>
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<tr>
<td>Local Coverage Determinations (LCD)</td>
<td>None</td>
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<tr>
<td>Local Coverage Article</td>
<td>None</td>
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<tr>
<td>KPWA Medical Policy</td>
<td>Due to the absence of a NCD, LCD, or other coverage guidance, KPWA has chosen to use their own Clinical Review Criteria, “Peroral Endoscopic Myotomy (POEM) for Esophageal Achalasia,” for medical necessity determinations. Use the Non-Medicare criteria below.</td>
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For Non-Medicare Members

There is insufficient evidence in the published medical literature to show that this service/therapy is as safe as standard services/therapies and/or provides better long-term outcomes than current standard services/therapies.

If requesting this service, please send the following documentation to support medical necessity:

- Last 3 months of clinical notes from requesting provider &/or consulting specialist.

Background

Esophageal achalasia (EA) is a rare esophageal motility disorder characterized by loss of peristalsis of the esophageal body and failure of the lower esophageal sphincter (LES) to relax in response to swallowing. The most common form of EA is idiopathic and the exact etiology for the disappearance of myenteric neurons that coordinate esophageal peristalsis and relaxation of LES is unknown. Esophageal achalasia results in retention of food and saliva in the esophagus leading to difficulty in swallowing, regurgitation, aspiration, chest pain, weight loss, and eventually irreversible dilatation of the esophageal body (Kumagai 2015, Patel 2016, Zhang 2016).

Esophageal achalasia is irreversible, and all current therapeutic interventions are palliative with the aim of reducing the pressure at the esophagogastric junction (EGJ), to facilitate the transit of food boluses into the stomach and reduce the related symptoms. Treatment options vary from pharmacotherapy (e.g. calcium channel antagonists and nitrates), botulinum toxin injection (BTI), endoscopic pneumatic dilatation (PD), surgical myotomy of the lower esophageal sphincter, to esophagogastrectomy for end-stage achalasia. Each of the therapeutic modalities has its indications, advantages, and limitations. e.g. pharmacological therapy does not have a durable effect and may be only suitable for patients with mild disease, elderly patients or those who cannot undergo more invasive treatment; BTI has a short-lived action; pneumatic dilatation is associated with symptom recurrence and post-
procedure gastroesophageal reflux (GERD); and surgical myotomy usually requires and additional fundoplication procedure to prevent GERD (Talukdar 2015, Marano 2016, Zhang 2016).

Currently laparoscopic Heller myotomy (LHM) is the treatment of choice for patients with esophageal achalasia who are fit for surgery. It provides superior and long-lasting symptom relief compared to other treatment modalities including pneumatic dilatation of the esophagus. LHM involves full thickness myotomy along the distal 4-6 cm of the esophagus and extending to 2-3 cm on to the gastric wall allowing the LES to remain open. LHM is usually followed by partial anterior fundoplication (Dor fundoplication). The procedure is minimally invasive, yet, the surgical access to the abdomen remains a potential source of wound infection, port-site hernia formation, and immediate postoperative pain (Kumagai 2015, Wei 2015, Morano 2016, Zhang 2016, Sanaka 2017, Docimo 2017, Kahrilis 2017).

Per-Oral Endoscopic Myotomy (POEM), was developed in Japan in 2008, and introduced into practice as a minimally invasive technique for the management of patients with achalasia. The procedure involves the creation of a submucosal tunnel followed by myotomy of the circular muscle layer to reduce pressure at the LES. It is performed under general anesthesia and consists of five major steps: 1. Patient position and planning endoscopy, 2. Entry into the submucosal space, 3. Creation of a submucosal tunnel, 4. Endoscopic myotomy of the circular muscles, and 5. Closure of the mucosal entrance. Unlike LHM which involves complete division of both circular and longitudinal LES muscle layers, POEM only cuts the inner, circular LES muscles maintaining the integrity of the longitudinal muscles. Thus, POEM has the potential advantages of both endoscopic dilatation and durable surgical myotomy in a single procedure (Talukdar 2015, Zhang 2016, Leeds 2017).

A major concern with POEM is the high rate of gastroesophageal reflux, which was observed in more than 50% of the patients undergoing the procedure despite the theoretical advantage of avoiding the esophagogastric junction dissection required for the LHM. Other reported serious adverse events associated with POEM include mucosal injury, esophageal perforation, major bleeding, pneumothorax, subcutaneous emphysema, pleural effusion, and pneumoperitoneum (Akintoye 2016, Kahrilas 2017).

Medical Technology Assessment Committee (MTAC)
Peroral Endoscopic Myotomy
12/15/2014:
Evidence Conclusion: Bhayani and colleagues compared the experience of 101 patients from a single institution undergoing either LHM or POEM. Swallowing outcomes at one and six months were assessed via objective measures (manometry and pH levels). In addition, the investigators collected information regarding operative time, complications and postoperative gastro-esophageal reflux disease (GERD). Manometry indicated that there were decreases in pressure across both groups, however, the postmyotomy resting pressures were higher for the POEM group than for LHMs (16 vs. 7 mm Hg, P=0.006). The same effect was not seen between groups for relaxation pressure (9 vs. 4). Both groups experienced relief of symptoms with the POEM group showing significantly lower Eckhardt scores when compared with the LHM group at one month (0.8 vs. 1.8, P<0.0001). At six months, however, the difference was no longer significant (1.7 vs. 1.2, P=0.1). Ultimately, the investigators conclude that POEM is comparable with LHM for safe and effective treatment of EA (Bhayani, Kurian et al. 2014). While POEM appears to be comparable to LHM, the technique is still evolving. At this particular point in time, the body of evidence only reports on the success of POEM in highly select populations with short-term follow-up. To add to this, the study is not randomized and relies on a small sample or subjects. Ultimately, the literature does not support the safety and effectiveness of POEM for the treatment of achalasia when compared to LHM. Conclusions: There is insufficient evidence to support the effectiveness of POEM compared to LHM for the treatment of EA. There is insufficient evidence to support the safety of POEM compared with LHM for the treatment of EA.

Articles: The literature search revealed over 200 studies relating to the use of POEM for the treatment of achalasia. The literature was dominated by publications that introduce and describe the technique as well as studies from individual centers describing their experience with POEM with short-term follow-up. A search of the clinicaltrials.gov website revealed several ongoing studies with the aim to evaluate of the clinical utility and safety of POEM (NCT01832779). For the purposes of this review, one of the larger and more recent nonrandomized comparison studies was identified for critical appraisal. The following articles were selected for critical appraisal: Bhayani NH, Kurian AA, Dunst CM, et al. A comparative study on comprehensive, objective outcomes of laparoscopic Heller myotomy with per-oral endoscopic myotomy (POEM) for achalasia. Annals of Surgery. 2014; 259(6): 1098-1103. See Evidence Table 1.
**Peroral Endoscopic Myotomy**

**Evidence Conclusion:** The literature search did not reveal any randomized controlled trials that compared POEM with laparoscopic Heller myotomy, the current standard of care; only noncompetitive case series and a small number of observational nonrandomized comparative studies and meta-analyses that pooled their results were identified. **Meta-analyses of comparative studies:** The published comparative studies identified by the search were relatively small observational studies that compared the outcomes of patients with esophageal achalasia treated POEM versus matched controls who had undergone treatment with LHM. The population sizes of the studies ranged from 8 patients to ~200 participants and there may be potential overlap between the studies published by the same groups of investigators. A number of systematic reviews with meta-analysis pooled the results of the majority of these studies three of which (Bhayani 2014, Ujiki 2013, and Hugeness 2013) were included in almost all meta-analyses. Based in the inclusion /exclusion criteria of the systematic reviews, smaller and/or studies with potentially overlapping population were added or excluded from the analyses. The overall pooled results of these comparative studies, none of which was randomized) as shown in **Evidence Table 1**, show no significant differences between the two procedures as regards their effect on reducing the achalasia symptoms as measured by the Eckardt score, perioperative pain score, complication rate, and length of hospital stay. POEM however, was associated with a significantly higher rate of symptomatic gastroesophageal reflux and esophagitis that required treatment. Based on these results some investigators concluded that the efficacy and safety of POEM appear to be comparable to those of LHM, and others (Wei and colleagues 2015) concluded that POEM achieves equivalent short-term outcomes compared to LHM. However, observational studies do not allow making any conclusion on the efficacy of POEM relative to LHM or other established treatments. The studies were only observational studies with potential bias and confounding. Patients were not randomly assigned the procedures, instead, POEM was compared to historical controls, the numbers of participants were small, with baseline differences in their characteristics, there were significant heterogeneity between the studies, and the follow-up duration was short, all of which limit generalization of the results. Large prospective randomized controlled trials with long-term outcomes are needed to determine the relative safety and efficacy of POEM and LHM. Schlotmann and colleagues’ 2017 systematic review and meta-analysis (Evidence Table 2) compared outcomes of POEM performed among different patient cohorts along the years (total N=1,958) versus LHM performed among a total of 5,834 participants. The studies included were not comparative; instead, the authors pooled the results of case series for each procedure and compared the overall summary results. This indirect comparison suggests that POEM may be more effective than LHM in reducing dysphagia symptoms in the short-term but is associated with a significantly higher incidence of pathologic reflux. These, similar to the results of other case series and nonrandomized studies, have to be interpreted with caution. **Non-comparative studies:** A large number of prospective and retrospective case series reported on the outcomes of the POEM procedure used for the management of patients with esophageal achalasia. The majority of the studies were conducted in Asia and included a small number of participants (<10-100 participants in each study). Only two case series included a little over 200 patients, and the largest reported on 500 consecutive patients treated in one center in Japan (Inoue 2015). In addition to these differences, other variations between the studies included differences in the patient characteristics, date and period the procedures were performed, technique used, length of myotomy, treatment success and other outcome measures, duration of follow-up, as well as other differences. A number of systematic review performing quantitative and qualitative analysis of the published case series were identified by the literature search (Barbieri 2015; Akintoye, 2016; and Crespin 2016). Akintoye and colleagues’ 2016 meta-analysis that was observed in Asian countries where the procedure had been introduced into practice earlier allowing for more development in its technique and acquisition of more skills by the interventionists. In addition, the outcomes of the studies were reported after variable follow-up durations and some e.g. symptoms relief, symptomatic gastroesophageal reflux, and esophagitis may be time dependent. Overall, the pooled results of the Akintoye’s meta-analysis as well as the non-comparative case series and their pooled results suggest that POEM may be effective in reducing dysphagia symptoms in the short-term among patients with esophageal achalasia. The POEM procedure, however, is associated with a high rate of symptomatic gastroesophageal reflux, esophagitis, and abnormal acid exposure. Reported perioperative adverse events of the procedure include mucosal injury, subcutaneous emphysema, pneumoperitoneum, and other serious events that occurred at a lower rate.
Conclusions

- The published literature is insufficient to determine the effects of POEM on the net health outcomes of patients with esophageal achalasia. The studies published to date, provide weak evidence on the short-term efficacy of POEM in reducing dysphagia symptoms in patients with esophageal achalasia, but on the expense of an increased rate of symptomatic gastroesophageal reflux and esophagitis.
- There is insufficient evidence to determine the long-term efficacy and safety of POEM for the management of patient with esophageal achalasia.
- The lack of randomized controlled trials, the small number of nonrandomized observational studies, design and quality of studies, short duration of follow-up, and significant variations between the studies in the surgical techniques and learning curve, operative time, definitions and reporting of the procedural success and adverse events, do not allow supporting the use of POEM as an alternative to LHM for the management of patients with esophageal achalasia.
- Long-term large randomized controlled trials are needed to determine the safety and efficacy of POEM in the management of patients with esophageal achalasia compared to other established procedures.
- Several RCTs comparing POEM to other established procedures is ongoing and may provide more evidence on its long-term safety and efficacy. Among these are the following:
  - Endoscopic Versus Laparoscopic Myotomy for Treatment of Idiopathic Achalasia: A Randomized, Controlled Trial: ClinicalTrials.gov Identifier: NCT01601678
  - Multi-center Study Comparing Endoscopic Pneumodilation and Peroral Endoscopic Myotomy (POEM). ClinicalTrials.gov Identifier: NCT01793922
  - Laparoscopy Heller Myotomy With Fundoplication Associated Versus Peroral Endoscopic Myotomy (POEM). ClinicalTrials.gov Identifier: NCT02138643

**Articles:** The literature search for recently published studies after the last MTAC review did not identify any randomized controlled trials that compared POEM with laparoscopic Heller myotomy or other standard treatments options. The published literature consisted of case series, non-randomized comparative studies, and a number of systematic reviews with quantitative meta-analyses (MAs) that pooled the results the published case series and/or nonrandomized comparative observational studies. Among these systematic reviews and meta-analyses were Barbieri, 2015, Talukdar 2015, Wei 2015, Akintoye 2016, Marano 2016, Patel 2016, Zhang 2016, Crespin 2017, Repici 2017, Schöttmann 2017, and Khan 2017. The latter examined the safety and efficacy of POEM for spastic esophageal disorders in general and was excluded from current review.

The use of Peroral Endoscopic Myotomy does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.