

MEDICAL POLICY		Peroral Endoscopic Myotomy (POEM)	
Effective Date: 7/1/2020  <div style="text-align: right;">7/1/2020</div>		Section: SUR	Policy No: 407
		Medical Policy Committee Approved Date: 12/17; 12/18; 2/19; 6/2020	
Medical Officer	Date		

See Policy CPT CODE section below for any prior authorization requirements

SCOPE:

Providence Health Plan, Providence Health Assurance, Providence Plan Partners, and Ayin Health Solutions as applicable (referred to individually as “Company” and collectively as “Companies”).

APPLIES TO:

All lines of business

BENEFIT APPLICATION

Medicaid Members

Oregon: Services requested for Oregon Health Plan (OHP) members follow the OHP Prioritized List and Oregon Administrative Rules (OARs) as the primary resource for coverage determinations. Medical policy criteria below may be applied when there are no criteria available in the OARs and the OHP Prioritized List.

DOCUMENTATION REQUIREMENTS

In order to determine the medical necessity of the request, the following documentation must be provided at the time of the request:

- Medical records to include documentation of all of the following:
 - Dysphagia with solids and liquids
 - History and all prior treatments
 - Gastroesophageal reflux disease (GERD) has been ruled out as the primary cause of dysphagia and/or heartburn
 - Upper endoscopy findings
 - Esophageal manometry findings
 - Timed barium esophagram findings if applicable
 - No evidence of malignancy (from upper endoscopy findings and/or endoscopic ultrasound with fine needle aspiration)

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POLICY CRITERIA

- I. Peroral endoscopic myotomy (POEM) to treat achalasia may be considered **medically necessary and covered** when **all** of the following criteria (A. – D.) are met:
 - A. Dysphagia with solids and liquids; **and**
 - B. Gastroesophageal reflux disease (GERD) has been objectively ruled out as the primary cause of dysphagia and/or heartburn by either of the following (a. or b.) when symptoms of heartburn are present:
 - a. Reflux and/or esophagitis is not present on endoscopy; **and/or**
 - b. 24-hour ambulatory esophageal pH monitoring rules out reflux.
 - C. Upper endoscopy with no evidence of pseudoachalasia or other reasons for mechanical obstruction or dysphagia; **and**
 - D. Either of the following are met (a. or b.):
 - a. Esophageal manometry has been performed. Findings reveal incomplete relaxation of the lower esophageal sphincter (integrated relaxation pressure above the upper limit of normal), and aperistalsis in the distal two-thirds of the esophagus; **or**
 - b. Esophageal manometry has been performed, with inconclusive findings and **both** of the following criteria (i. and ii.) are met:
 - i. Modified esophagram with timed emptying of a standardized barium volume (also known as “timed barium esophagram”) has been performed. Findings reveal dilation of the esophagus, narrow esophagogastric junction, aperistalsis, and/or delayed emptying of barium; **and**
 - ii. Esophagogastric malignancy has been ruled out by appropriate means (e.g., upper endoscopy, endoscopic ultrasound with fine needle aspiration).

- II. Peroral endoscopic myotomy (POEM) to treat achalasia may be considered **medically necessary and covered** following a failed laparoscopic Heller myotomy.

- III. Peroral endoscopic myotomy (POEM) is considered **investigational and is not covered** as a treatment for any other indication, including but not limited to:
 - A. Achalasia not meeting criteria I. or II. above
 - B. Dysphagia in the absence of achalasia not meeting criteria I. or II. above
 - C. Gastroesophageal reflux
 - D. Diffuse esophageal spasm
 - E. Distal esophageal spasm

MEDICAL POLICY	Peroral Endoscopic Myotomy (POEM)
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- F. Jackhammer (hypercontractile) esophagus
 - G. Gastroparesis
 - H. Other esophageal disorders
- Link to [Policy Summary](#)

CPT CODES

All Lines of Business	
<p>Unlisted Codes</p> <p>All unlisted codes will be reviewed for medical necessity, correct coding, and pricing at the claim level. If an unlisted code is billed related to services addressed in this policy then it will be denied as not covered.</p>	
43499	Unlisted procedure, esophagus

DESCRIPTION

Achalasia

Achalasia is an uncommon motility disorder affecting the sphincters of the gastrointestinal tract, most commonly occurring in the lower esophageal sphincter (LES). It is characterized by a progressive inflammatory degeneration of ganglion cells in the esophageal wall that eventually results in gastrointestinal tract disruption. The cause in primary achalasia is unknown. Progression is quite slow and it is typical for patients to experience symptoms for years prior to seeking medical care. The clinical differential is complex and misdiagnoses is common, leading to treatment for other disorders including gastroesophageal reflux disease (GERD) for a number of years prior to correctly identifying achalasia.

When the LES fails to relax as is the case in achalasia patients, it is often accompanied by a loss of peristalsis in the distal esophagus. Diagnostic evaluations include suspecting those with dysphagia to solids and liquids; heartburn unresponsive to a trial of proton pump inhibitor (PPI) therapy; retained food in the esophagus on upper endoscopy; and unusually increased resistance to passage of an endoscope through the esophagogastric junction (EGJ). While dysphagia with both solids and liquids is the most common symptom of the achalasia, regurgitation of undigested food, chest pain, weight loss, nocturnal cough, and heartburn may also be indicators, hence the complex differential due to significant overlap with other more common conditions.^{1,2} Achalasia treatment is aimed at decreasing the resting pressure in the LES to allow passage of ingested material.

Peroral Endoscopic Myotomy

Peroral endoscopic myotomy (POEM) is an endoscopic technique that emerged in the past decade as a minimally invasive management option for achalasia.³ POEM is a form of natural orifice transluminal endoscopic surgery (NOTES) considered to be an endoscopic equivalent to surgical myotomy. The POEM procedure allows for myotomy of the lower esophageal muscles to be performed via mucosal incision and entry into the submucosa of the esophagus, thus eliminating the need for direct incisions.

Surgical myotomy, particularly Heller myotomy performed laparoscopically (known as laparoscopic Heller myotomy [LHM]), is currently the standard interventional treatment option for patients with achalasia. Another interventional procedure commonly used to treat achalasia is pneumatic dilation of the lower esophageal sphincter. The POEM procedure combines the minimal invasiveness of pneumatic dilation with the therapeutic goal of a surgical myotomy.

Although POEM was developed for achalasia, it has recently been proposed as a potential treatment for other disorders, including spastic esophageal disorders as well as conditions like gastroesophageal reflux. In addition, the POEM procedure has been adapted to be performed in the stomach (termed gastric peroral endoscopic pyloromyotomy or G-POEM) for the treatment of gastroparesis.

REVIEW OF EVIDENCE

A review of the ECRI, Hayes, Cochrane, and PubMed databases was conducted regarding the use of the POEM procedure as a treatment for any indication. Below is a summary of the most recent available evidence identified through April 2020. The evidence review is primarily focused on systematic reviews, RCT's, and comparative nonrandomized studies published after the former.

Achalasia

The Eckardt symptom score is often reported as an outcome measure of therapeutic success in the literature evaluating POEM treatments. There are 4 components to the score, based on self-reported symptom severity and weight loss.^{4,5} Weight loss (none, <5 kg, 5-10kg, or >10kg), dysphagia (none, occasional, daily, or each meal), chest pain (none, occasional, daily, or each meal), and regurgitation (none, occasional, daily, or each meal) are given a score of 0-3 based on patient reported responses. The results vary from 0 to 12, with a result of ≤ 3 often defining clinical success. When the ESS was assessed for validity and reliability in a well-defined patient population, the dysphagia and regurgitation items were found to perform the most consistently.⁶ However, timing of assessment (i.e., initial administration and subsequent follow-up) was identified as a potentially problematic for the score overall, and half of the items were identified as being not related to standard physiological assessment of achalasia severity.

Given the pathophysiology of achalasia and accompanying symptomology, esophageal manometry to evaluate swallowing and status of dysphagia are the preferred outcomes of interest.

Systematic Reviews

In 2019, Hayes published an updated comparative effectiveness review, evaluating POEM as a treatment for esophageal achalasia versus laparoscopic Heller myotomy (LHM) or pneumatic dilation (PD).⁷ The review included 19 studies comparing POEM with either LHM (15 studies)⁸⁻²², PD (3 studies)²³⁻²⁵, or both (1 study)²¹. Enrollment ranged from 50 to 241 patients; follow-up time ranged up to 60 months following intervention. As in previous reports on this topic, the Hayes authors concluded that the evidence base is of poor quality: 14 included studies were rated poor quality, 4 were rated fair quality, and 1 study was rated good quality (RCT reported by Ponds et al. in 2019 comparing POEM to PD²⁵). The low-quality evidence from the generally poor-quality studies suggest that POEM is a safe procedure (sixteen studies found no major complications related to POEM). Nine of 13 studies comparing POEM to LHM reported no difference in perioperative complications or did not provide statistical comparisons;

the remaining 4 studies favored POEM over LHM. The evidence base also suggests that outcomes for patients with achalasia treated with POEM may be achieved with similar efficacy when compared to LHM and PD. In shorter follow-up, differences in patients lost to follow-up and outcomes related to symptom relief were found to be similar. Of studies with the longest available follow-up (median, 36.2-158.1 weeks), five studies of POEM vs LHM reported no statistically significant difference between symptom relief.

The Hayes report also included data from seven recent systematic reviews with meta-analyses comparing POEM to LHM.²⁶⁻³² In general, these reviews reported that POEM was comparable to LHM for most outcomes including the Eckardt score, as well as for adverse events including incidence of perforation, hospital length of stay and operative time. Numerous systematic reviews reported incidence of GERD as being a significant cost following POEM as compared to LHM and PD. Authors of systematic reviews noted limitations of studies included in their meta-analyses to include a general lack of comparator groups, overlapping patient populations, heterogeneity in procedure and techniques, discrepancy in follow-up times between comparator groups when present, and short-term follow-up times across the evidence base. All of the studies noted the need for additional randomized comparative studies of LHM and POEM, though overall the reviews recognized the POEM procedure as being relatively safe and effective.

In 2018, ECRI published an evidence review evaluating the safety and efficacy of POEM for the treatment of achalasia.³³ Having systematically searched the literature through January 2018 according to pre-defined criteria, ECRI included 5 systematic reviews and meta-analyses, 1 RCT, 3 non-randomized cohort studies and 5 case series for review. Outcomes of interest were symptom resolution at one year follow-up, symptom resolution compared to patients receiving laparoscopic Heller myotomy (LHM), recurring symptoms following surgery, and adverse events.

All of the included studies reported positive results for the primary reported outcome of symptom resolution (Eckardt score <3). Three cohort studies (n = 242) and one meta-analysis, evaluating 23 studies (n = 2,373), reported symptom resolution one-year follow-up in >98% of patients treated with POEM. Compared to LHM, two meta-analyses (77 studies; n = 8,278) and three nonrandomized studies (n = 244) reported comparable or superior symptom resolution among patients receiving POEM, similar or fewer complications, shorter operative times, similar or longer hospital stays, but a greater risk of GERD onset. One systematic review (36 studies, n = 2,373) reported GERD symptoms in 9% of patients at a median eight-month follow-up after POEM. Across three cohort studies (n = 1,874) and one systematic review (n = 1,122), serious adverse events were reported in 1% to 6% of patients. Only one RCT and five case series reported on procedure success, symptoms, complications, and GERD medication use in patients treated with POEM at three-year follow-up. ECRI concluded that a large body of evidence exists, which indicates that POEM is a safe and effective for treating achalasia.

In 2019, Evensen and colleagues published a systematic review evaluating the efficacy of POEM in treatment-naïve achalasia patients.³⁴ Independent reviewers systematically identified eligible studies, assessed quality, and extracted data. Outcomes of interest were symptom score and objective testing (i.e. high resolution manometry (HRM) or timed barium esophagogram (TBE)). Having searched the literature through November 2017, investigators ultimately included 7 studies (6 retrospective cohort studies; 1 prospective cohort study) for review. Sample sizes ranged from 32 to 100 patients and follow-up ranged from 3 to 51 months. All studies reported a short-term clinical success rate of >90% (defined as an Eckardt score ≤3). HRM was applied pre- and post-surgery in all of the included studies, each

reporting significant decreases in lower-esophageal pressure. Only two studies included their TBE protocol with barium height analysis. Strengths of this study include the systematic review of literature following a pre-defined protocol and evaluation of methodological quality by two independent reviewers. Limitations of the study are centered on the quality of the studies included for review. Each study suffered from small sample sizes, low follow-up rates, the limited application of objective tests, retrospective study designs, and the low-middle income treatment setting (i.e. China) for 6 out of the 7 reviewed studies. Given these limitations, investigators concluded that “a definite conclusion of the effect of POEM in treatment-naïve patients can at present hardly be drawn.”

Randomized Controlled Trials (RCTs)

In 2019, Werner et al., reported results of a multicenter, randomized trial comparing POEM (N=112) to LHM plus Dor’s fundoplication (N=109) in patients with symptomatic achalasia.³⁵ The primary outcome of interest was Eckardt symptom score of 3 or less without the use of treatments at the 2-year follow-up. One hundred eight of 112 patients in the POEM group and 104 of 109 patients in the LHM group had complete follow-up data available with respect to the primary end point. In 83.0% of patients the predefined clinical success was observed in the POEM group, as well as 81.7% of patients in the LHM group (difference, 1.4 percentage points; 95% confidence interval [CI], -8.7 to 11.4; P = 0.007 for pre-specified noninferiority which was identified to be a margin of the lower bound being above -12.5 percentage points). Subgroup exploratory analyses of patient groups (i.e., by achalasia subtype) did not report measures of statistical significance in between-group comparisons. Amongst secondary outcomes reported, the incidence of reflux esophagitis (all grades) was higher in the POEM group than the LHM group at 3 months (57% vs. 20%; odds ratio, 5.74; 95% CI, 2.99 to 11.00) and at 24 months (44% vs. 29%; odds ratio, 2.00; 95% CI, 1.03 to 3.85). Esophageal pH monitoring was reported as similar proportions of patients with abnormal reflux between groups without statistical significance for comparison reported. The use of proton-pump inhibitors was higher in the POEM group than the LHM group across time after baseline. The authors reported limitations of due to surgical experience – those performed LHM plus Dor’s fundoplication were more experienced than the endoscopists were at performed POEM. Additionally, less than 50 percent of eligible patients were enrolled due to refusal to consent to randomization. Given that blinding was not possible, patient’s reports of outcomes may have been biased. The authors concluded that, overall, their results suggest no between group difference in improvements in patient-reported quality of life at 2-years following POEM and LHM, and POEM is noninferior to LHM in controlling symptoms of achalasia, but resulted in higher incidence of GERD.

Nonrandomized Comparative Studies

No additional nonrandomized comparative studies of relevance were identified that were not already included in the above summarized systematic reviews.

Gastroparesis

A review of the evidence found no RCTs or systemic reviews evaluating POEM for the treatment of gastroparesis. Despite reporting symptom relief, non-randomized clinical trials studies to date suffer from small sample sizes (n=7 to 47), heterogeneous patient cohorts, a lack of comparator groups and inadequate follow-up (≤18 months).³⁶⁻⁴⁵

Other Indications for POEM

Systematic Reviews

In 2017, Khan and colleagues published results from their systematic review and meta-analysis evaluation POEM for the treatment of spastic esophageal disorders (SEDs) – including spastic achalasia (type III), diffuse esophageal spasm (DES), and nutcracker/jackhammer esophagus (JH).⁴⁶ Searching the literature through January 2016, independent reviewers systematically identified eligible studies, assessed quality, and extracted data. Outcomes of interest were weighted pooled rates for clinical success (defined as Eckardt scores ≤ 3), severity of dysphagia based on a health-related quality of life questionnaire, and adverse events (AEs). Clinical success rates and AEs were calculated using fixed- or random-effects models based on heterogeneity. Eight observational studies, with sample sizes varying from 3 months to 3 years, were ultimately included for review.

The patient cohort across all eight studies (n=179) included 116 patients with type III achalasia, 37 patients with JH, and 18 patients with DES. Using the National Institutes of Health quality assessment tool, investigators assessed 2 studies of the 8 studies to be “good quality” and 6 to be “fair quality.” Cumulative clinical success of POEM for the treatment of all SEDs was 87% (78, 93%; 95% CI), $I^2 = 37\%$. Adverse events of POEM in all SEDs was calculated to be 14% (9, 20%; 95%CI), $I^2 = 0\%$, with no difference in safety among individual SEDs.

All studies included for review suffered from small sample sizes, lack of long-term follow-up, and non-randomized observational study designs. Validity is further undermined by investigators’ inability to evaluate differences in clinical outcomes based on patient demographics. Investigators concluded that larger, prospective studies are required before POEM complements or replaces Heller myotomy in the treatment of SEDs.

Nonrandomized Studies

In 2018, Khashab and colleagues conducted a multi-center retrospective study evaluating POEM for the treatment of non-achalasia esophageal motility disorders.⁴⁷ In total, 50 patients (56% female; mean age 61.7 years) underwent POEM at 11 centers for esophagogastric junction outflow obstruction (EGJO), diffuse esophageal spasm (DES) and jackhammer esophagus (JE). Follow-up ranged from 6 to 9 months. Outcomes of interest were rates or technical success, clinical response (Eckardt scores ≤ 3) and adverse events. Mean Eckardt score decreased from 6.2 to 1.0 in EGJO ($p < 0.001$) and from 6.9 to 1.9 in DES/JE ($p < 0.001$). A total of 9 (18%) adverse events occurred, rated as mild in 55.6% and moderate in 44.4%. Limitations include the study’s small sample size, retrospective design, and inadequate follow-up. Investigators concluded that randomized trials were needed to confirm the safety and efficacy of POEM for non-achalasia esophageal motility disorders.

CLINICAL PRACTICE GUIDELINES

American Gastroenterological Association (AGA)

In 2017, the AGA published a clinical practice update, evaluating POEM for the treatment of achalasia.⁴⁸ Having conducted a comprehensive literature review, investigators recommended POEM be “considered as a treatment option of comparable efficacy to [laparoscopic Heller myotomy], albeit with no long-term

outcomes data and minimal controlled outcomes data currently available.”⁴⁸ Investigators also noted that POEM patients are at high-risk for developing reflux esophagitis and may require medical management post-procedure to manage symptoms.

American College of Gastroenterology (ACG)

The ACG’s 2013 clinical guideline on the diagnosis and management of achalasia discusses POEM as an emerging therapy and concluded that the available evidence from prospective cohort studies indicates POEM has promise as an alternative to the laparoscopic approach.² However, the panel noted that randomized prospective comparison trials with standard approaches are needed, and POEM should only be performed in the context of clinical trials with the understanding that effective alternatives are available.

Society of the American Gastrointestinal and Endoscopic Surgeons (SAGES)

SAGES’ most recent guidelines for the surgical treatment of achalasia were published in May 2011 and include evidence from a literature search done in October 2009.¹ The statement describes POEM as a technique in its infancy and concluded that more experience is needed before recommendations can be provided.

American Society for Gastrointestinal Endoscopy (ASGE)

In 2020, the ASGE published updated evidence-based guidelines on the management of achalasia.⁴⁹ Recommendations were developed by expert panel with regard to the certainty of the evidence, the balance of benefits and harms of the management option, assumptions about the values and preferences associated with the decision along with available data on resource utilization, and cost effectiveness. The strength of the aggregate individual recommendation is based on the overall evidence quality and an assessment of the anticipated benefits and harms. All panel members approved the following recommendations:

1. Laparoscopic Heller myotomy, pneumatic dilation, and POEM are effective therapeutic modalities for patients with achalasia. Decision between these treatment options should depend on achalasia type, local expertise, and patient preference. ⊕⊕⊕⊕
2. We recommend against the use of botulinum toxin injection as definitive therapy for achalasia patients. Botulinum toxin injection may be reserved for patients who are not candidates for other definitive therapies. ⊕⊕⊕○
3. We suggest POEM as the preferred treatment for management of patients with type III achalasia. ⊕○○○
4. In patients with failed initial myotomy (POEM or laparoscopic Heller myotomy), we suggest pneumatic dilation or redo myotomy using either the same or an alternative myotomy technique (POEM or laparoscopic Heller myotomy). ⊕○○○
5. We suggest that patients undergoing POEM are counseled regarding the increased risk of postprocedure reflux compared with pneumatic dilation and laparoscopic Heller myotomy. Based on patient preferences and physician expertise, postprocedure management options include objective testing for esophageal acid exposure, long-term acid suppressive therapy, and surveillance upper endoscopy. ⊕⊕○○

6. We recommend pneumatic dilation compared with botulinum toxin injection for patients with achalasia. ⊕⊕⊕⊕
7. We recommend that laparoscopic Heller myotomy and pneumatic dilation are comparable treatment options for management of patients with achalasia types I and II, and the treatment option should be based on shared decision-making between the patient and provider.
8. We suggest that POEM and laparoscopic Heller myotomy are comparable treatment options for management of patients with achalasia types I and II, and the treatment option should be based on shared decision-making between the patient and provider. ⊕⊕ ○○

CENTERS FOR MEDICARE & MEDICAID

As of May 2020, no Centers for Medicare & Medicaid (CMS) coverage guidance was identified which addresses peroral endoscopic myotomy (POEM) as a treatment for any esophageal disorder or gastroparesis.

POLICY SUMMARY

There is enough research to show that peroral endoscopic myotomy (POEM) may be an effective management option for select individuals with achalasia. Studies have demonstrated short term safety and efficacy equivalent to laparoscopic Heller myotomy for this minimally invasive option. Patients may also be at high-risk for developing reflux esophagitis and may require medical management post-procedure to manage symptoms. Despite this, the American Gastroenterological Association (AGA) and American Society for Gastrointestinal Endoscopy (ASGE) both recommended that POEM be considered as an option for the treatment of achalasia.

There is not enough research to show that peroral endoscopic myotomy (POEM) is a safe and effective option for treatment of any other esophageal disorder or gastroparesis. The evidence base is predominantly comprised of nonrandomized studies of heterogeneous populations with short-term follow-up. No evidence-based clinical practice guidelines recommend POEM as a treatment for gastroparesis or esophageal disorders other than achalasia.

INSTRUCTIONS FOR USE

Company Medical Policies serve as guidance for the administration of plan benefits. Medical policies do not constitute medical advice nor a guarantee of coverage. Company Medical Policies are reviewed annually and are based upon published, peer-reviewed scientific evidence and evidence-based clinical practice guidelines that are available as of the last policy update. The Companies reserve the right to determine the application of Medical Policies and make revisions to Medical Policies at any time. Providers will be given at least 60-days notice of policy changes that are restrictive in nature.

The scope and availability of all plan benefits are determined in accordance with the applicable coverage agreement. Any conflict or variance between the terms of the coverage agreement and Company Medical Policy will be resolved in favor of the coverage agreement.

REGULATORY STATUS

Mental Health Parity Statement

Coverage decisions are made on the basis of individualized determinations of medical necessity and the experimental or investigational character of the treatment in the individual case.

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