Prior Authorization Review Panel
MCO Policy Submission

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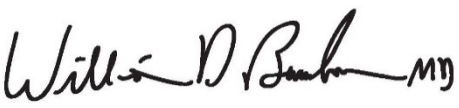
Plan: Keystone First	**Submission Date**: April 29, 2019
Policy Number: CCP.1195	**Effective Date:** October 1, 2015 **Revision Date:** April 2, 2019
Policy Name: Gastric electrical stimulation	
Type of Submission – Check all that apply: ☐**New Policy** ☑**Revised Policy*** ☐**Annual Review – No Revisions**	
***All revisions to the policy must be highlighted using track changes throughout the document.** **Please provide any clarifying information for the policy below:** Please see revisions below using tracked changes.	
Name of Authorized Individual (Please type or print): William D. Burnham, MD	**Signature of Authorized Individual:** 

Keystone First

Coverage by Vista Health Plan,
an independent licensee of the Blue Cross and Blue Shield Association.

Clinical Policy Title: Gastric electrical stimulation

Clinical Policy Number: CCP.1195

Effective Date:	**October 1, 2015**
Initial Review Date:	September 17, 2015
Most Recent Review Date:	April 2, 2019
Next Review Date:	April 2020

Related policies:

None.

Policy contains:

- Gastric electrical stimulation.
- Gastroparesis.
- Neuromodulation.
- Obesity.

ABOUT THIS POLICY: *Keystone First has developed clinical policies to assist with making coverage determinations. Keystone First's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Keystone First when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Keystone First's clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Keystone First's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Keystone First will update its clinical policies as necessary. Keystone First's clinical policies are not guarantees of payment.*

Coverage policy

Keystone First considers the use of gastric electrical stimulation using the Enterra® Therapy system (Medtronic Inc., Minneapolis, Minnesota) to be clinically proven and, therefore, medically necessary for either of the following clinical indications:

- Treatment of chronic, intractable (drug-refractory) nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology. An institutional review board must approve the use of gastric electrical stimulation for this purpose to ensure it will be used in accordance with the humanitarian device exemption indication granted by the U.S. Food and Drug Administration.
- Revision, replacement, or removal of a previously approved implantation for complications associated with gastric electrical stimulation (e.g., infection, lead dislodgement, or lead erosion into the small intestine).

Keystone First considers use of the Maestro® Rechargeable System (EnteroMedics Inc., St. Paul, Minnesota) for treatment of obesity to be investigational, and, therefore, not medically necessary, as improvement in clinical outcomes has not been demonstrated in this population.

Limitations:

The patient must be age 18 years or older.

Gastric electrical stimulation is contraindicated in any patient whom the physician determines is not a candidate for surgical procedures and/or anesthesia due to physical or mental conditions.

Because Enterra is U.S. Food and Drug Administration-approved for use under a humanitarian device exemption, the manufacturer may request documentation of institutional review board approval to ensure regulatory compliance.

Use of magnetic resonance imaging is contraindicated for persons with an implantable gastric electrical stimulation device, as it is not compatible with the neurostimulator and leads.

Use of diathermy in an individual with an implanted gastric electrical stimulation device is contraindicated, because the energy produced by diathermy can be transferred through the implant system or any of the device components. This may contribute to tissue damage that could result in severe injury or death. Diathermy can also damage parts of the gastric electrical stimulation device.

The gastric electrical stimulation system may be affected by, or may adversely affect, cardiac pacemakers or therapies, cardioverter defibrillators, electrocautery, external defibrillators, ultrasonic equipment, radiation therapy, theft detectors, and screening devices.

Gastric electrical stimulation is not medically necessary for use in children and pregnant women, as the safety and effectiveness of this device has not been established in these populations.

All other uses of gastric electrical stimulation are not medically necessary, including, but not limited to:

- As an initial treatment for gastroparesis.
- For treatment of cyclic vomiting syndrome.
- For treatment of diabetes mellitus in persons without gastroparesis.
- For treatment of gastrointestinal dysmotility disorders other than gastroparesis.

Alternative covered services:

- Surgical intervention (e.g., venting gastrostomy, gastrojejeunostomy, pyloroplasty and gastrectomy).
- Antiemetic or prokinetic drug therapy.

Background

Synchronization and propagation of gastric contraction is essential to normal gastric function (Mintchev, 2013). Gastric electrical activity is a complex phenomenon resulting in gastric motility, which in turn leads to gastric emptying. Hypothetically, if gastric electrical signals are disturbed in their propagation pattern, then the gastric motility of the organ would be affected. Using this logic, a variety of gastric motility disorders, including gastroparesis, could be treated by facilitating existing electrical disturbances to improve gastric motility. Conversely, normally synchronized gastric electrical signals may be disturbed deliberately, inducing delay in gastric emptying leading to early satiety and weight loss.

Gastroparesis is the incomplete emptying of the stomach resulting from autonomic nervous system dysfunction. Gastroparesis is characterized by scintigraphic evidence of delayed gastric emptying in the absence of mechanical obstruction. Sentinel symptoms of gastroparesis include early satiety, postprandial fullness, nausea, vomiting, bloating, and upper abdominal pain (Camilleri, 2011). In severe and chronic cases, patients may suffer dehydration, poor nutritional status, and poor glycemic control (i.e., persons with diabetes). Diabetic (29 percent), idiopathic (36 percent), and postsurgical (13 percent) etiologies comprise the majority of cases in the tertiary referral setting (Hyett, 2009). Gastroparesis significantly impacts health-related quality of life, increases direct health care costs through hospitalizations, emergency room and doctor visits, and is associated with morbidity and mortality (Camilleri, 2011).

Medical management of gastroparesis includes dietary changes, anti-emetics and prokinetics, but many of these medications are associated with unwanted side effects that limit their use. Enteral or total parenteral nutrition may be required in severe cases. Surgical management (e.g., insertion of a gastrostomy tube and/or feeding jejunostomy tube, pyloroplasty, gastrectomy, or gastrojejunostomy) may be required in cases of medically refractory gastroparesis (Camilleri, 2011).

During the past 20 years, there has been a dramatic increase in obesity in the United States, and rates remain high. More than one-third of U.S. adults (34.9 percent) and approximately 17 percent (or 12.7 million) of children and adolescents ages 2 – 19 years have obesity (Centers for Disease Control and Prevention, 2015). Treatments for obesity include dietary and lifestyle changes, pharmacotherapy and/or behavior modification, and bariatric surgery (Mintchev, 2013). Gastric electrical stimulation has been proposed as a surgical alternative for treating gastroparesis that remains refractory to medical management and for treating obesity in adults who have not achieved adequate results with a supervised weight loss program.

Gastric electrical stimulation:

Gastric electrical stimulation applies an implantable electrical stimulator that provides mild electrical stimulation to the lower stomach nerves. An electrical stimulator (pulse generator) is inserted either by laparoscopy or laparotomy into a subcutaneous pocket and connects to unipolar leads (electrodes) that are sutured to the greater curvature of the stomach muscle. An external stimulator programmer is used to set or adjust the settings or to turn the stimulator on and off. The procedure can be done on an inpatient or outpatient basis and is reversible.

Two types of gastric electrical stimulation have been developed (Bortolotti, 2011):

- Low-frequency/high-energy gastric electrical stimulation with long pulse stimulation, also called gastric pacing, which uses frequencies just above that of the native slow wave with a pulse duration of tenths of a second. Its efficacy for improving gastric emptying and vomiting is limited, and it requires batteries too heavy and large to be implanted in a patient for long-term treatment.
- High-frequency/low-energy gastric electrical stimulation with short pulse stimulation, also called gastric neurostimulation or neuromodulation, which uses frequencies markedly above that of the native slow wave with pulse duration less than one thousandth of a second, delivered singly or in bursts of various length. Sequential neural gastric electrical stimulation is able to induce propagated gastric contractions with consequent acceleration of gastric emptying. It is the most promising method, as it affects the core of the problem of gastroparesis, which is gastric stasis, rather than just mitigating the symptoms. By consuming low power, this system does not require unwieldy batteries and allows the implantation of a portable device.

The U.S. Food and Drug Administration (2014; 2015)has approved two high-frequency/low-energy gastric electrical stimulation devices:

- The Enterra Therapy system — approved in 2014 for the treatment of chronic, intractable (drug-refractory) nausea and vomiting secondary to gastroparesis of diabetes or idiopathic etiology (not postsurgical etiologies) under a humanitarian use device designation, meaning it is a medical device for use in the treatment of medical conditions that affect fewer than 4,000 individuals per year (see 21CFR814.3). Enterra is contraindicated in any patient whom the physician determines is not a candidate for surgical procedures and/or anesthesia due to physical or mental conditions. The safety and effectiveness of this system has not been evaluated in patients under age 18 or over age 70 years, or in pregnant women.
- The Maestro Rechargeable System — approved as a Class 3 neuromodulator for obesity in January, 2015 (product code PIM). Maestro delivers high-frequency electrical stimuli to gastric vagal trunks, causing intermittent intra-abdominal vagal nerve impulses between the brain and the stomach. Maestro is indicated for adults age 18 years or older who have not achieved adequate results with a supervised weight loss program and who have a body mass index ≥ 40 – 45 kg/m^2, or ≥ 35 – 39.9 kg/m^2 plus an obesity-related health condition. The list of contraindications is extensive and includes concurrent chronic pancreatic disease, portal hypertension, and/or esophageal varices; a history of Crohn's disease and/or ulcerative colitis; pulmonary embolism or blood coagulation disorders; clinically significant hiatal hernias; or a history of bariatric surgery, fundoplication, gastric resection, or major upper-abdominal surgery.

Searches

Keystone First searched PubMed and the databases of:

- UK National Health Services Center for Reviews and Dissemination.
- Agency for Healthcare Research and Quality and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services.

We conducted searches on February 19, 2019. Searched terms were: "gastric electrical stimulation," "gastroparesis" (MeSH), and "electric stimulation therapy" (MeSH).

We included:

- Systematic reviews, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- Guidelines based on systematic reviews.
- Economic analyses, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

Findings

For this policy Keystone First identified one overview of systematic reviews/meta-analyses (National Institute for Health and Care Excellence, 2013) and two evidence-based guidelines (Camilleri, 2013; National Institute for Health and Care Excellence, 2014) of gastric electrical stimulation for treatment of persons with gastroparesis, and one randomized controlled trial for treatment of obesity (Ikramuddin, 2014). No economic analyses met criteria for inclusion for either indication.

Multichannel stimulation devices are promising because they require a fraction of the energy used in single channel pacing and may allow for a propagated electrical and contractile sequence, which enhances results. However, to date, there has been only a single clinical trial with 20 patients, and no results have been reported.

Although the evidence in support of gastric electrical stimulation is weak due to poor study design and inconsistent results, it may be an attractive treatment option for patients who have exhausted available medical treatment options and are refractory to treatment, who suffer with debilitating symptoms, and who wish to avoid less invasive (i.e., surgical) interventions.

Medically refractory gastroparesis:

The overall quality of the evidence is low to moderate with a high risk of bias and at times conflicting results. The evidence consists of mostly uncontrolled observational studies or industry-sponsored, open-label controlled studies. All studies used the Enterra system.

There is insufficient evidence to establish definitive patient selection criteria for use of gastric electrical stimulation in patients with medically refractory gastroparesis, and there is no consensus or societal guideline to inform on the selection of patients (e.g., failed therapeutic trials or level of nutritional compromise) as compassionate treatment. The study base comprised adult patients with symptomatic and scintigraphically-confirmed gastroparesis that is refractory to prokinetic and/or antiemetic medication. The majority had diagnoses of diabetic gastric neuropathy, idiopathic gastroparesis, and postsurgical gastroparesis. Exclusion criteria varied among studies and commonly included the presence of any known structural cause of symptoms, psychogenic vomiting, chemical dependency, previous gastric surgery, and pregnancy.

Gastric electrical stimulation was associated with improvement in vomiting symptoms, the need for nutritional support, and health-related quality of life in some patients. Gastric electrical stimulation improves gastric emptying in some patients, but patients with diabetic gastroparesis appear to show the greatest response. Length of follow-up was variable, but 12 months was preferred in the majority of studies. According to the manufacturer, possible side effects of gastric electrical stimulation may include gastrointestinal symptoms, abdominal pain, feeding tube complications, difficulty swallowing, dehydration, acute diabetic complications, and loss of therapeutic effect (Medtronic, 2017).

Safety data were reported inconsistently, but overall gastric electrical stimulation appears to be a safe procedure. According to the manufacturer, implanting the gastric electrical stimulation system carries with it the same risks as those associated with other gastric surgery (e.g., infection, allergic response to implanted materials, temporary or permanent neurologic complications, pain at the surgery site, bruising at the implantation site, and bleeding) (Medtronic, 2017). Death was rare and occurred in three percent (2/72) of treated patients due to small bowel infarction and heart failure. In approximately 10 percent of the cases, the device had to be replaced, repositioned, or removed. The main reasons were infection at the implant site and lack of symptom improvement. Other less common reasons included lead dislodgements, small bowel obstruction caused by wires, penetration of electrode into lumen of the stomach, erosion through the skin, device migration, and pain at the implantation site.

Evidence-based guidance supports limited use of gastric electrical stimulation for treating patients with medically refractory symptoms of gastroparesis, particularly nausea and vomiting, based on a moderate level of evidence. The American College of Gastroenterology issued a conditional recommendation for considering gastric electrical stimulation for compassionate treatment in patients with refractory symptoms, particularly nausea and vomiting (Camilleri, 2013). Symptom severity and gastric emptying have been shown to improve in patients with diabetic gastroparesis, but not in patients with idiopathic or postsurgical gastroparesis, based on moderate quality evidence.

According to the National Institute for Health and Care Excellence (2014), current evidence on the efficacy and safety of gastric electrical stimulation is adequate to support its use with normal arrangements for clinical governance, consent, and audit. Gastroparesis can be a very debilitating condition with very few treatment options, and additional data about the effects of the procedure on symptoms in the long term and on device durability would be useful. Therefore, clinicians should fully inform patients regarding the benefits and risks of complications, which can be serious, including the need to remove the device. Patient

selection, the implantation procedure, and follow-up should take place within specialist gastroenterology units with expertise in gastrointestinal motility disorders .

Obesity:

For treatment of obesity, the best evidence supporting the use of gastric electrical stimulation, and on which FDA approval was based, is from the ReCharge Study (Ikramuddin, 2014; Clinicaltrials.gov identifier: NCT01327976). In this multi-site randomized clinical trial, 162 patients received the Maestro RC2 System VBLOC device, and 77 received a sham device. Participants had a body mass index of 40 to 45 kg/m^2, or 35 to 40 kg/m^2 and at least one obesity-related condition. The first efficacy objective was to demonstrate a mean percent excess weight loss (comparison between groups achieving superiority with a 10 percentage-point margin. The second was to demonstrate that at least 55 percent of participants in the treatment group would achieve a 20 percent excess weight loss and 45 percent would achieve a 25 percent excess weight loss. The primary safety objective was to determine a serious adverse event rate related to device, procedure, or therapy in the treatment group of less than 15 percent.

Although excess weight loss was greater in the treatment group (highly statistically significant at $P = 0.002$ for treatment difference in a post-hoc analysis), neither efficacy objective was met. However, the primary safety objective was met with a serious adverse event rate of 3.7 percent (95 percent confidence interval 1.4 percent to 7.9 percent, $P < 0.001$) in the treatment group. Mild or moderate heartburn or dyspepsia and abdominal pain attributed to therapy were more frequent in the vagal nerve block group.

Policy updates:

Singh (2015) examined the effects of temporary gastric electrical stimulation in gastroparesis-like syndrome in patients showing symptoms of gastroparesis with non-delayed gastric emptying. The benefits of temporary gastric electrical stimulation relative to permanent gastric electrical stimulation are fewer side effects such as infection, lead dislodgement, and migration of the device, as well as the ability to predict the treatment effect before committing to permanent gastric electrical stimulation. Temporary gastric electrical stimulation improved nausea, vomiting, and total symptom scores without accelerating gastric emptying. However, they did not consider abdominal pain, another common symptom of gastroparesis, as a parameter after insertion of the temporary gastric electrical stimulation electrode pair and neurostimulator. The authors also opined that their technique provides pivotal information regarding the decision to adopt permanent gastric electrical stimulation for patients with refractory gastroparesis.

One systematic review carried out a meta-analysis of 49 studies of mixed designs of gastric electrical stimulation for gastroparesis and found substantial discrepancies between the reported results of controlled and open label gastric electrical stimulation studies (Levinthal, 2016). A strong placebo effect and referral bias likely contributed to these findings.

An analysis of the U.S. Food and Drug Administration's Manufacturer and User Device Experience database of adverse effects of the Enterra system voluntarily reported between January, 2001, and October, 2015, identified 1,587 entries (Bielefeldt, 2017). The most common problems were related to lack or loss of

efficacy, followed by pain or complications affecting the pocket site. More than one-third (35.7 percent) of the reported adverse events prompted surgical correction. These results and the questionable benefits of gastric electrical stimulation argue against using gastric electrical stimulation outside of clinical trials. These conclusions are consistent with the previous policy findings and warrant no policy changes.

We did not identify any relevant new publications in the 2018 review.

In 2019, the policy ID changed from 08.02.03 to CCP.1195. We did not identify any recent relevant publications for inclusion.

References

Professional society guidelines/other:

Camilleri M, Parkman HP, Shafi MA, et al. Clinical guideline: management of gastroparesis. *Am J Gastroenterol*. 2013 Jan; 108(1): 18 – 37; quiz 8. Doi: 10.1038/ajg.2012.373.

Medtronic, Inc. Gastric electrical stimulation. About the therapy. Updated April, 2017. https://www.medtronic.com/us-en/healthcare-professionals/therapies-procedures/digestive-gastrointestinal/gastric-electrical-stimulation/education-training/about-the-therapy.html . Accessed March 6, 2018.

National Institute for Health and Care Excellence (NICE). Gastroelectrical stimulation for gastroparesis. NICE interventional procedures guidance [IPG489]. Issued May 2014. London, UK. NICE website. https://www.nice.org.uk/guidance/ipg489. Accessed February 20, 2019.

Office of the Federal Register. Title 21 – Food and drugs. Part 814 – Premarket approval of medical devices. 21CFR814.3. Electronic Code of Federal Regulations (e-CFR). Government Publishing Office. Updated January 21, 2019. https://www.ecfr.gov/cgi-bin/text-idx?SID=1a068e4263b247c18edf5727abc49e7c&mc=true&node=pt21.8.814&rgn=div5. Accessed February 20, 2019.

Peer-reviewed references:

Camilleri M, Bharucha AE, Farrugia G. Epidemiology, mechanisms, and management of diabetic gastroparesis. *Clin Gastroenterol Hepatol*. 2011; 9(1): 5-12; quiz e7. Doi: 10.1038/ajg.2012.373.

Centers for Disease Control and Prevention (CDC). Adult obesity facts. Reviewed August 13, 2018. https://www.cdc.gov/obesity/data/adult.html. Accessed February 20, 2019.

Enterra Therapy System (formerly named Gastric Electrical Stimulation (GES) System) — H990014. U.S. Food and Drug Administration website. Updated February 18, 2019.

https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfhde/hde.cfm?id=375491. Accessed February 20, 2019.

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Hyett B, Martinez FJ, Gill BM, et al. Delayed radionucleotide gastric emptying studies predict morbidity in diabetics with symptoms of gastroparesis. *Gastroenterology*. 2009 Aug; 137(2): 445-452. Doi: 10.1053/j.gastro.2009.04.055.

Lal N, Livemore S, Dunne D, Khan I. Gastric electrical stimulation with the Enterra System: a systematic review. *Gastroenterol Res Pract.* 2015; 2015: 762972. Doi: 10.1155/2015/762972.

Mintchev M. Gastric electrical stimulation for the treatment of obesity: from entrainment to bezoars—a functional review. *ISRN Gastroenterol*. 2013: 434706. Doi: 10.1155/2013/434706.

Singh S, McCrary J, Kedar A, et al. Temporary endoscopic stimulation in gastroparesis-like syndrome. *J Neurogastroenterol Motil.* 2015; 21: 520-527. Doi: 10.5056/jnm15046.

Centers for Medicare & Medicaid Services National Coverage Determination:

No National Coverage Determininations identified as of the writing of this policy.

Local Coverage Determinations:

No Local Coverage Determinations identified as of the writing of this policy.

Commonly submitted codes

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

CPT Code	Description	Comment
43647	Laparoscopy, surgical; implantation or replacement of gastric neurostimulator electrodes, antrum.	
43648	Laparoscopy, surgical; revision or removal of gastric neurostimulator electrodes, antrum.	
43881	Implantation or replacement of gastric neurostimulator electrodes, antrum, open.	
43882	Revision or removal of gastric neurostimulator electrodes, antrum, open.	

CPT Code	Description	Comment
64590	Insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling.	
64595	Revision or removal of peripheral or gastric neurostimulator pulse generator or receiver.	
95980	Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient measurements) gastric neurostimulator pulse generator/transmitter; intraoperative, with programming.	
95981	Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient measurements) gastric neurostimulator pulse generator/transmitter; subsequent, without reprogramming.	
95982	Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient measurements) gastric neurostimulator pulse generator/transmitter; subsequent, with reprogramming.	

ICD-10 Code	Description	Comment
K31.84	Gastroparesis	

HCPCS Level II Code	Description	Comment
N/A		