Title: Gastric Electrical Stimulation

Description/Background

Gastric electrical stimulation (GES) is performed using an implantable device designed to treat chronic drug-refractory nausea and vomiting secondary to gastroparesis of diabetic, idiopathic, or postsurgical etiology. GES has also been investigated as a treatment of obesity. The device may be referred to as a gastric pacemaker.

GASTROPARESIS

Gastroparesis is a chronic disorder of gastric motility characterized by delayed emptying of a solid meal. Symptoms include bloating, distension, nausea, and vomiting. When severe and chronic, gastroparesis can be associated with dehydration, poor nutritional status, and poor glycemic control in diabetic patients. While most commonly associated with diabetes, gastroparesis is also found in chronic pseudo-obstruction, connective tissue disorders, Parkinson’s disease, and psychological pathologic conditions. Some cases may not be associated with an identifiable cause, and are referred to as idiopathic gastroparesis. Treatment of gastroparesis includes prokinetic agents, (eg, metoclopramide) and antiemetic agents (eg, metoclopramide, granisetron, ondansetron). Severe cases may require enteral or total parenteral nutrition.

Treatment

Gastric electrical stimulation, also referred to as gastric pacing, using an implantable device, has been investigated primarily as a treatment for gastroparesis. Currently available devices consist of a pulse generator, which can be programmed to provide electrical stimulation at different frequencies, connected to intramuscular stomach leads, which are implanted during laparoscopy or open laparotomy.
OBESITY
GES has also been investigated as a treatment of obesity. It is used to increase a feeling of satiety with subsequent reduction in food intake and weight loss. The exact mechanisms resulting in changes in eating behavior are uncertain but may be related to neurohormonal modulation and/or stomach muscle stimulation.

Regulatory Status:

In 2000, the Gastric Electrical Stimulator system (now called Enterra™ Therapy System; Medtronic) was approved by the U.S. Food and Drug Administration (FDA) through the humanitarian device exemption process (H990014) for the treatment of gastroparesis. The GES system consists of 4 components: the implanted pulse generator, 2 unipolar intramuscular stomach leads, the stimulator programmer, and the memory cartridge. With the exception of the intramuscular leads, all other components have been used in other implantable neurologic stimulators, such as spinal cord or sacral nerve stimulation. The intramuscular stomach leads are implanted either laparoscopically or during a laparotomy and are connected to the pulse generator, which is implanted in a subcutaneous pocket. The programmer sets the stimulation parameters, which are typically set at an “on” time of 0.1 second alternating with an “off” time of 5.0 second.

Currently, no GES devices have been approved by FDA for the treatment of obesity. The Transcend® (Transneuronix; acquired by Medtronic in 2005), an implantable gastric stimulation device, is available in Europe for treatment of obesity.

Medical Policy Statement

Gastric pacing for the treatment of morbid obesity is experimental/investigational. The safety and effectiveness of this procedure have not been established.

Gastric electrical stimulation for the treatment of gastroparesis is experimental/investigational. The safety and effectiveness of this procedure have not been established.

Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

N/A

CPT/HCPCS Level II Codes (Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)

Established codes:
N/A
Other codes (investigational, not medically necessary, etc.):

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Rationale

GASTRIC ELECTRICAL STIMULATION FOR GASTROPARESIS

Systematic Reviews
Several systematic reviews of studies on gastric electrical stimulation (GES) for gastroparesis have been published,(1-3) the most recent and comprehensive of which is by Levinthal et al (2017).(1) To be selected for the Levinthal review, studies had to include adults with established gastroparesis, report patient symptom scores and administer treatment for at least 1 week. Five randomized controlled trials (RCTs) and 13 non-RCTs meeting criteria were identified. Pooled analysis of data from the 5 RCTs (n=185 patients) did not find a statistically significant difference in symptom severity when the GES was turned on versus off (standardized mean difference [SMD], 0.17; 95% confidence interval [CI], -0.06 to 0.40; p=0.15). Another pooled analysis did not find a statistically significant difference in nausea severity scores when the GES was on or off (SMD, -0.143; 95% CI, -0.50 to 0.22; p=0.45). In a pooled analysis of 13 open-label single-arm studies and data from open-label extensions of 3 RCTs, mean total symptom severity score decreased 2.68 (95% CI, 2.04 to 3.32) at follow-up from a mean of 6.85 (95% CI, 6.28 to 7.42) at baseline. The rate of adverse events in the immediate postoperative period (reported in 7 studies) was 8.7% (95% CI, 4.3% to 17.1%). The in-hospital mortality rate within 30 days of surgery was 1.4% (95% CI, 0.8% to 2.5%), the rate of reoperations (up to 10 years of follow-up) was 11.1% (95% CI, 8.7% to 14.1%), and the rate of device removal was 8.4% (95% CI, 5.7% to 12.2%).

Randomized Controlled Trials
Representative crossover RCTs are described next. Abel et al (2003) reported findings from the Worldwide Anti-Vomiting Electrical Stimulation Study (WAVESS).(4) This double-blinded crossover study initially described in a Food and Drug Administration materials, included 33 patients with intractable idiopathic or diabetic gastroparesis.(5) The primary endpoint was a reduction in vomiting frequency, as measured by patient diaries. In the initial phase of the study, all patients underwent implantation of the stimulator and were randomly and blindly assigned to stimulation on or stimulation off for the first month, with crossover to off and on during the second month. Baseline vomiting frequency was 47 episodes per month, which declined in both on and off groups to 23 to 29 episodes, respectively. However, no significant differences were found in the number of vomiting episodes between the 2 groups, suggesting a placebo effect. In the second, open-label, phase of the trial, all patients had their stimulators turned on for the remainder of the 6- to 12-month follow-up. During this period, vomiting frequency declined in both the idiopathic and diabetic subgroups.

McCallum et al (2010) reported on a crossover RCT evaluating GES (Enterra device) in patients with chronic intractable nausea and vomiting from diabetic gastroparesis (DGP).(6) In this trial, 55 patients with refractory DGP (5.9 years of DGP) were given Enterra implants. After surgery, all patients had the stimulator turned on for 6 weeks and then were randomized to groups that had consecutive 3-month cross-over periods with the device on or off. After this
period, the device was turned on in all patients, and they were followed up unblinded for 4.5 months. During the initial 6-week phase with the stimulator turned on, the median reduction in weekly vomiting frequency (WVF) compared with baseline was 57%. There was no significant difference in WVF between patients who had the device turned on or off during the 3-month crossover period. At 1 year, the WVF of all patients was significantly lower than baseline values (median reduction, 68%; \( p<0.001 \)). One patient had the device removed due to infection; 2 patients required surgical intervention due to lead-related problems.

McCallum et al (2013) evaluated GES (Enterra system) in patients with chronic vomiting due to idiopathic gastroparesis in a randomized, double-blind crossover trial.(7) In this trial, 32 patients with nausea and vomiting associated with idiopathic gastroparesis, unresponsive or intolerant to prokinetic and antiemetic drugs, received Enterra implants and had the device turned on for 6 weeks. Subsequently, 27 of these patients were randomized to have the device turned on or off for 2 consecutive 3 month periods. Twenty-five of these subjects completed the randomized phase; of note, 2 subjects had the device turned on early, 2 subjects had randomization assignment errors, and 1 subject had missing diaries. During the initial 6 week on period, all subjects demonstrated improvements in their weekly vomiting frequency, demonstrating a median reduction of 61.2% (5.5 episodes/week) compared with baseline (17.3 episodes/week; \( P<0.001 \)). During the on-off crossover phase, subjects demonstrated no significant differences between the on and off phase for the study’s primary endpoint, median weekly vomiting frequency (median 6.4 in on-phase vs 9.8 in off-phase; \( P=1.0 \)). Among the 19 subjects who completed 12 months of follow up, there was an 87.1% reduction in median weekly vomiting frequency (2 episodes/week) compared with baseline (17.3 episodes/week; \( p<0.001 \)). Two subjects required surgical intervention for lead migration/dislodgement or neurostimulator migration.

Section Summary: Gastric Electrical Stimulation for Gastroparesis
Five crossover RCTs have been assessed GES for treating gastroparesis. A 2017 meta-analysis of these 5 RCTs did not find a significant benefit of GES on the severity of symptoms associated with gastroparesis. Patients generally reported improved symptoms at follow-up whether or not the device was turned on, suggesting a placebo effect. For example, there was no significant difference in the on versus off position in symptom severity or nausea severity scores.

GES FOR OBESITY
A single RCT has evaluated the use of GES for treating obesity: the SHAPE trial. In 2009, Shikora et al reported on a double-blind RCT evaluating GES obesity.(8) All 190 trial participants received an implantable gastric stimulator and were randomized to have the stimulator turned on or off. All patients were evaluated monthly, participated in support groups, and reduced their dietary intake by 500 kcal/d. At 12-month follow-up, there was no statistically significant difference in excess weight loss between the treatment group (weight loss, 11.8%) and the control group (weight loss, 11.7%) using intention-to-treat analysis (\( p=0.717 \)).

Small case series and uncontrolled prospective trials (2002-2004) have reported positive outcomes for weight loss and maintenance of weight loss along with minimal complications.(9-14) However, interpretation of these uncontrolled studies is limited.
ONGOING AND UNPUBLISHED CLINICAL TRIALS
Some currently unpublished trials that might influence this review are listed in Table 1.

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NCT: national clinical trial.

*: Denotes industry-sponsored or cosponsored trial.

SUMMARY OF EVIDENCE
For individuals who have gastroparesis who receive gastric electrical stimulation (GES), the evidence includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are symptoms and treatment-related morbidity. Five crossover RCTs have been published. A 2017 meta-analysis of these 5 RCTs did not find a significant benefit of GES on the severity of symptoms associated with gastroparesis. Patients generally reported improved symptoms at follow-up whether or not the device was turned on, suggesting a placebo effect. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have obesity who receive GES, the evidence includes a RCT. Relevant outcomes are change in disease status and treatment-related morbidity. The SHAPE trial did not show significant improvement in weight loss with GES compared with sham stimulation. The evidence is insufficient to determine the effects of the technology on health outcomes.

Supplemental Information

CLINICAL INPUT RECEIVED FROM PHYSICIAN SPECIALTY SOCIETIES AND ACADEMIC MEDICAL CENTERS
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

2015 Input
In response to requests, BCBSA received input from 1 specialty society (2 reviewers) and 4 academic centers while this policy was under review in 2015. Most respondents agreed that GES should be considered investigational for gastroparesis. There was a lack of consensus whether GES should be considered medically necessary for any specific indication (eg, diabetic gastroparesis, idiopathic gastroparesis, gastroparesis of postsurgical etiology). The reviewers were not asked about GES for treatment of obesity.

2009 Input
In response to requests, BCBSA received input from 4 academic medical centers (5 reviewers) while this policy was under review in 2009. There was strong agreement among reviewers about the limited data for use of GES in diabetic and idiopathic gastroparesis and about the
need for RCTs. There was strong agreement that GES is investigational in the treatment of obesity.

PRACTICE GUIDELINES AND POSITION STATEMENTS

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (2014) has issued guidance on gastroelectrical stimulation for gastroparesis.(15) The institute made the following recommendations:

• Current evidence on the efficacy and safety of gastric electrical stimulation for gastroparesis is adequate to support the use of this procedure with normal arrangements for clinical governance, consent and audit.
• …clinicians should inform patients considering gastric electrical stimulation for gastroparesis that some patients do not get any benefit from it. They should also give patients detailed written information about the risk of complications, which can be serious, including the need to remove the device.
• Patient selection and follow-up should be done in specialist gastroenterology units with expertise in gastrointestinal motility disorders, and the procedure should only be performed by surgeons working in these units.

American College of Gastroenterology

The American College of Gastroenterology published practice guideline on the management of gastroparesis in 2013.(16) The college recommended that:

“GES may be considered for compassionate treatment in patients with refractory symptoms, particularly nausea and vomiting. Symptom severity and gastric emptying have been shown to improve in patients with DG [diabetic gastroparesis], but not in patients with IG [idiopathic gastroparesis] or PSG [postsurgical gastroparesis]. [Conditional recommendation (there is uncertainty about trade-offs), moderate level of evidence (further research would be likely to have an impact on the confidence in the estimate of effect).]"

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS

Not applicable

Government Regulations

National:
There is no National Coverage Determination for gastric electrical stimulation for the treatment of gastroparesis or morbid obesity.

Local:
There is no Local Coverage Determination for gastric electrical stimulation for the treatment of gastroparesis or morbid obesity.

The Enterra™ Therapy System (Medtronic®) has received approval through a “humanitarian device exemption” from the U.S. Food and Drug Administration (FDA). Therefore, this device is covered for Medicare beneficiaries for the treatment of chronic, intractable (drug refractory) nausea and vomiting secondary to gastroparesis of diabetic or idiopathic etiology in patients age 18 to 70 years.
(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

N/A

References


*The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 4/3/18, the date the research was completed.*
### Joint BCBSM/BCN Medical Policy History

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Next Review Date: 4th Qtr, 2019
BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: GASTRIC ELECTRICAL STIMULATION

I. Coverage Determination:

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II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.