

Medical Policy



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Title: Gastric Electrical Stimulation

Professional

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DESCRIPTION

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

Currently, only one gastric electrical stimulator has received approval from the U.S. Food and Drug Administration (FDA) (see note below), the Gastric Electrical Stimulator (GES) system (now called Enterra™ Therapy System), manufactured by Medtronic. 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 sec alternating with an "off" time of 5.0 sec.

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. Treatment of gastroparesis includes prokinetic agents, such as metoclopramide, and antiemetic agents, such as metoclopramide, granisetron, or ondansetron. Severe cases may require enteral or total parenteral nutrition.

Gastric electrical stimulation has also been investigated as a treatment of obesity as a technique to increase a feeling of satiety with subsequent reduced food intake and weight loss. The exact mechanisms resulting in changes in eating behavior are uncertain but may be related to neuro-hormonal modulation and/or stomach muscle stimulation. There are no gastric electrical stimulation devices approved by the FDA for the treatment of obesity. The Transcend® Implantable Gastric Stimulation device, manufactured by Transneuronix Corporation and acquired by Medtronic in 2005, is currently available in Europe for treatment of obesity. Medtronic announced in December 2005 that the preliminary results of the Screened Health Assessment and Pacer Evaluation, or SHAPE trial, which was initiated by Transneuronix using the Transcend device, "did not meet the efficacy endpoint of a difference in mean excess weight loss at one year."

Note:

It should be noted that the GES system received FDA approval through a humanitarian device exemption (HDE). This regulatory category was established in 1996 and only applies to devices intended to benefit fewer than 4,000 patients. The approval process is similar to that of a premarket approval application (PMA) but is exempt from the effectiveness requirements of a PMA. Thus the application is not required to include results of scientifically valid clinical investigations but must contain sufficient information for the FDA to determine that the device does not pose unreasonable or significant risk of illness or injury. A humanitarian use device may only be used in facilities that have an institutional review board (IRB) to supervise clinical testing of the device.

POLICY

- A. Gastric electrical stimulation is considered **experimental / investigational** for the treatment of gastroparesis of diabetic, idiopathic, or post-surgical etiology.
- B. Gastric electrical stimulation is considered **experimental / investigational** for the treatment of obesity.

RATIONALE**Gastroparesis**

The evidence on gastric electrical stimulation (GES) for gastroparesis consists of 2 small randomized crossover trials, and numerous case series. The case series include several that report on medium and/or long-term use (greater than 1 year of follow-up) of the device.

Systematic reviews

In a 2012 systematic review and meta-analysis, Chu and colleagues (1) evaluated 10 studies on GES for the treatment of gastroparesis. Included in the meta-analysis were 2 randomized controlled trials (RCT) by Abell (2) and McCallum (3), both et al. and 8 observational studies, totaling 601 patients who received GES for more than 1 month. The treatment arms of the RCTs were combined with the single-arm case series to give summary estimates of treatment effect. This review did not attempt to evaluate the RCTs separately from the case series and, therefore, did not attempt to make conclusions on the efficacy of GES compared to a control group.

The meta-analysis found gastric electrical stimulation significantly improved scores for total symptom severity, nausea severity, and vomiting severity. Gastric emptying times at 2 and 4 hours also significantly improved. In the sub-analysis of 197 patients with diabetic gastroparesis, total symptom severity scores and gastric emptying at 2 and 4 hours significantly improved. In the sub-analysis of 65 patients with idiopathic gastroparesis, total symptom severity scores and gastric emptying at 4 hours significantly improved but not at 2 hours. In the sub-analysis of 40 patients with post-surgical gastroparesis, total symptom severity scores and gastric emptying at 2 hours significantly improved but not at 4 hours. A sub-analysis of nausea and vomiting severity scores was not presented. Infection (3.87%) was the most common complication followed by device migration (2.69%) and pain at the site of implant (0.67%). Other infrequent complications (1.18%) included peptic ulcer disease, electrode penetration of the stomach lumen, erosion of the skin after abdominal wall trauma, and implant wire-related small bowel obstruction. While this meta-analysis found GES provided significant benefit in gastroparesis treatment, interpretation of results must be made with caution, since the majority of studies analyzed were low-quality observational studies. Only 2 studies had control groups, and the control groups of these RCTs were not included in the combined analysis.

Randomized, controlled trials

The data presented to the U.S. Food and Drug Administration (FDA) documenting the "probable benefit" of the GES system was based on a multicenter, double-blinded crossover study, the Worldwide Anti-Vomiting Electrical Stimulation Study (WAVESS). (4) The study included 33 patients with intractable idiopathic or diabetic gastroparesis. The primary endpoint of the study 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. The baseline vomiting frequency was 47 episodes per month, which significantly 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.

The final results of the WAVESS study were reported in 2003, which allows further review of the data. (2) When looking individually at those with idiopathic gastroparesis, there was a similar drop in vomiting frequency compared to baseline regardless of whether the device was turned on or off, suggesting a placebo effect. In contrast, in those with diabetic gastroparesis, compared to baseline, there was a small drop in vomiting frequency with the device turned off, compared to a larger drop in vomiting frequency with the device turned on. In the second open-label phase of the trial, all patients had their stimulators turned on for the remainder of the 6 to 12 months' follow-up. During this period, the vomiting frequency declined in both the idiopathic and diabetic subgroups. The cause of this continuing decline is uncertain, related to either a placebo effect or some sort of long-term effect of gastric stimulation.

McCallum and colleagues performed a multicenter prospective study to evaluate GES (Enterra therapy) in patients with chronic intractable nausea and vomiting from diabetic gastroparesis (DGP). (3) In this study, 55 patients with refractory DGP (5.9 years of DGP) were given implants of the Enterra system. After surgery, all patients had the stimulator turned on for 6 weeks and then were randomly assigned 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 difference in WVF between patients who had the device turned on or off during the 3-month cross-over period. At 1 year, the WVF of all patients was significantly lower than baseline values (median reduction, 68%; p less than 0.001). One of the patients had the device removed due to infection; 2 patients required surgical intervention due to lead-related problems.

Conclusions. Two small, crossover RCTs have been performed on GES for gastroparesis. In addition to being small in numbers, these RCTs have methodologic limitations including the use of a crossover design that may limit the ability to maintain successful

blinding. In each RCT, patients in both of the treatment groups improved, but it is not possible to determine whether the improvement was due to GES treatment or due to a placebo effect.

Case series

Anand and colleagues reported on 214 consecutive drug-refractory patients with the symptoms of gastroparesis (146 idiopathic, 45 diabetic, 23 after surgery) who consented to participate in a variety of clinical research and clinical protocols at 3 centers from January 1992 through January 2005, resulting in 156 patients implanted with a GES device and 58 patients as controls. (5) At last follow-up (median 4 years), most patients who received implants (135 of 156) were alive with intact devices, significantly reduced gastrointestinal symptoms, and improved health-related quality of life, with evidence of improved gastric emptying. Also, 90% of the patients had a response in at least 1 of 3 main symptoms. Most patients who were explanted, usually for pocket infections, were later re-implanted successfully.

In a case series of 12 patients receiving a gastric stimulation device, Abell and colleagues reported rapid improvement in nutritional parameters (e.g., body mass index, serum albumin). (6) Forster and colleagues reported on their experience at a single institution among 55 patients with gastroparesis, as documented by gastric retention. (7) While the total symptom score improved, gastric emptying did not change. The authors reported significant improvements in upper gastrointestinal symptoms, health-related quality of life, nutritional status, glucose control, and hospitalizations at 6 and 12 months in a retrospective review of 48 adult patients with diabetes who received a gastric electrical stimulation implant. (6) The review also noted that gastric emptying was not significantly faster. Similarly, van der Voort and colleagues reported that 17 patients with diabetic gastroparesis experienced a decrease in nausea and vomiting and an improvement in glucose control in a prospective case series examining the 12-month outcomes. (8)

Several trials were identified that evaluated the use of a temporary gastric stimulator. Temporary stimulators are intended to be used to determine whether or not an individual patient will respond to GES prior to undertaking a permanent implant. Abell et al. (9) performed a trial of temporary GES in 58 patients with 1 of 3 etiologies (idiopathic, diabetic, postsurgical). A temporary device was placed in all patients with the device turned on or off for 4 consecutive days, followed by cross-over to the other group for an additional 4-day period. The frequency of vomiting decreased in both groups. At day 3, the decrease in vomiting was significantly greater for the GES group; however, by day 8, the differences between groups were no longer significant.

Andersson et al. (10) tested a temporary GES in 27 patients with drug-refractory nausea/vomiting. Fourteen patients were treated with temporary GES in open-label fashion, and 13 had a randomized, cross-over trial in which the device was turned on for 12-14 days and off for 12-14 days. These authors reported that the majority of patients (22/27) improved following GES placement. Of the 13 patients in the randomized cross-

over phase, 6 had improvement in symptoms during the on period and 7 did not. Of the 7 patients who did not improve during the on period, there was improvement with an increased intensity of stimulation.

Elfvin et al. (11) treated 3 children with intractable vomiting who were younger than 3-years-old with a temporary GES. There were no adverse events of GES placement. All 3 children responded to the temporary GES and were implanted with a permanent device. Following permanent placement, all 3 children reported at least a 50% reduction in vomiting episodes.

The durability of GES treatment was evaluated in several publications. Lin and colleagues reported on outcomes beyond 3 years in patients receiving GES for gastroparesis. (12) Of 55 patients, 10 died of non-pacemaker-related complications, 6 had the devices removed, and 2 could not be reached. In the remaining 37 patients, symptoms, hospital days, and the use of medications had sustained reductions (from baseline) beyond 3 years. Mason and colleagues reported on the 20-month follow-up of 27 of 29 patients referred for gastrectomy who instead received GES for refractory gastroparesis. (13) Three patients required additional procedures due to poor outcomes. Nutritional support was discontinued in the 19 patients who were dependent on supplemental feeding prior to the procedure. Gastric emptying rates improved. While these results are encouraging, given the findings of the WAVESS study, randomized trials are needed to determine the efficacy of GES in gastroparesis.

McCallum et al. reported on long-term follow-up for 188 patients who received a GES and had at least 1 year of follow-up visits. (14) This sample was drawn from a total of 221 patients treated with a GES system between 1 and 11 years prior to the study. The authors report that symptoms, hospitalizations, and medication use all improved over the time period of the study. The percent of patients with at least 50% improvement in symptoms was 58% for diabetic patients, 53% for postsurgical gastroparesis, and 48% for idiopathic disease. A total of 13 patients (7%) had their device removed due to infection.

Conclusions. Numerous case series and uncontrolled studies on GES have been published. These studies generally report improvements in symptoms following treatment. However, this evidence is insufficient to draw conclusions because of the lack of control groups and the possibility that improvement is due to a placebo effect and/or other non-specific factors.

Obesity

There has only been 1 RCT published on GES for the treatment of obesity: the SHAPE trial. In 2009, Shikora and colleagues reported on a randomized, controlled, double-blind study to evaluate GES for the treatment of obesity. (15) All 190 patients participating in the study 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 diet by 500-kcal/day. At 12 months follow-up, there was no difference in excess weight loss between the treatment group (weight loss of 11.8% +/- 17.6%) and the control group (weight loss of 11.7% +/- 16.9%) using intention-to-treat analysis (P = .717).

Small case series and uncontrolled prospective trials have reported positive outcomes in weight loss and maintenance of weight loss along with minimal complications. (16-21) However, interpretation of these uncontrolled studies is limited. In conclusion, given the available evidence including the results of the SHAPE RCT, GES for the treatment of obesity is considered investigational.

Ongoing Clinical Trials

A search of online site ClinicalTrials.gov identified 1 randomized double-blind cross-over study of gastric electrical stimulation (NCT00903799). In this study, health and healthcare utilization outcomes will be evaluated in 220 patients with diabetes, idiopathic or post-surgical related refractory nausea and vomiting. This study is expected to be completed in October 2013.

Clinical Input Received through Physician Specialty Societies and Academic Medical Centers

In response to requests, input was received through no physician specialty societies and 4 academic medical centers (5 reviewers) while this policy was under review for May 2009. 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. There was strong agreement among reviewers about the limited data for use of GES in diabetic and idiopathic gastroparesis and about the need for randomized controlled studies. There was strong agreement that GES is investigational in the treatment of obesity.

Summary

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

The evidence on the efficacy of gastric electrical stimulation to treat gastroparesis is inadequate to permit scientific conclusions. Only 2 small randomized studies have been published on the treatment of gastroparesis. In one randomized study, only 33 patients recruited from 11 centers in the United States were included. There was no statistically significant improvement in symptoms for the entire study group compared to placebo, but positive results were reported for the subgroup of 17 patients with diabetic

gastroparesis. In the other randomized study of 55 patients, while weekly vomiting frequency was significantly lower than baseline values at 1-year follow-up, there was no difference in weekly vomiting frequency between patients who had the device turned on or off during the 3-month cross-over period. The case series report improvements in symptoms, nutritional parameters, and quality of life. However, the lack of a control group precludes the conclusion that these changes are due to treatment with gastric electrical stimulation, given the variable natural history of gastroparesis, and the expected placebo effect. In conclusion, gastric electrical stimulation for the treatment of gastroparesis of diabetic, idiopathic, or post-surgical etiologies is considered investigational.

There has only been 1 published randomized study on gastric electrical stimulation for the treatment of obesity (the SHAPE trial) which did not show any improvement in weight loss with gastric electrical stimulation. Case series publications are limited and insufficient to draw conclusions on health outcomes. Given the results of the SHAPE trial, gastric electrical stimulation for the treatment of obesity is considered investigational.

Practice Guidelines and Position Statements

The National Institute for Clinical Excellence issued guidance on gastroelectrical stimulation for gastroparesis in 2004. (22) This guidance indicates there is insufficient evidence to support gastroelectrical stimulation for gastroparesis outside of audit or research purposes.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. 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.

CPT/HCPCS

43647	Laparoscopy, surgical; implantation or replacement of gastric neurostimulator electrodes, antrum
43648	Laparoscopy, surgical; revision or removal of gastric neurostimulator electrodes, antrum
43659	Unlisted laparoscopy procedure, stomach
43881	Implantation or replacement of gastric neurostimulator electrodes, antrum, open
43882	Revision or removal of gastric neurostimulator electrodes, antrum, open
43999	Unlisted procedure, stomach
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
L8680	Implantable neurostimulator electrode, each (implant requires 2 leads)
L8685	Implantable neurostimulator pulse generator, single array, rechargeable, includes extension
L8686	Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension
L8687	Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
L8688	Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension

- There are CPT codes that are specific to insertion of the gastric stimulation device: 43647, 43648, 43881, 43882, 64590, 64595.
- There are also specific codes for electronic analysis and programming of gastric neurostimulator pulse generator: 95980, 95981.
- The CPT code book instructs that after January 1, 2012, laparoscopic procedures related to gastric stimulation electrodes for morbid obesity should be reported using code 43659 and laparotomy procedures related to gastric stimulation electrodes for morbid obesity should be reported using 43999.
- The insertion of the gastric neurostimulator pulse generator is coded with 64590 and revision or removal of the pulse generator is coded with 64595, regardless of the indication.
- The following HCPCS codes may be used: L8680, L8685, L8686, L8687, L8688.

Diagnoses

Experimental / Investigational for all diagnoses related to this medical policy.

REVISIONS

12-02-2013	Policy added to the bcbks.com web site on 10-31-2013 for an effective date of 12-02-2013 for professional and institutional.
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