Enterra® Therapy

FOR CHRONIC NAUSEA AND VOMITING SECONDARY TO GASTROPARESIS

enterra medical®

Hope and help for your gastroparesis patients

Enterra® Therapy is the first and only device shown to reduce nausea and vomiting secondary to gastroparesis through Gastric Electrical Stimulation (GES).

Enterra Therapy is indicated for the treatment of chronic intractable (drug refractory) nausea and vomiting secondary to gastroparesis and may be appropriate for patients who:

- **have difficulty managing nausea and vomiting symptoms, despite having tried firstline therapies of diet modification and medications**
- **are 18-70 years of age**

More than

patients worldwide

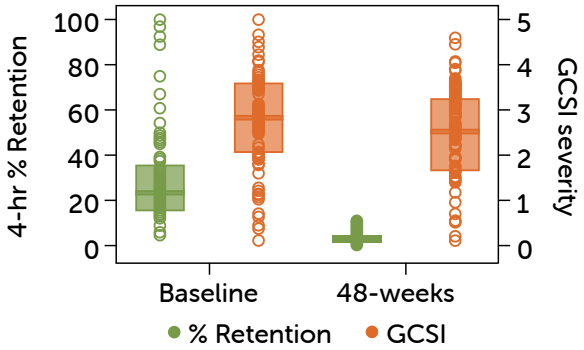
have received Enterra Therapy to help resume everyday activities, like taking their seat back at the table.

Enterra Therapy does not work for everyone. Any combination of diet modification, medication, nutritional support, surgery, and Enterra Therapy may be necessary to control symptoms of gastroparesis.

Gastroparesis is more than a motility issue

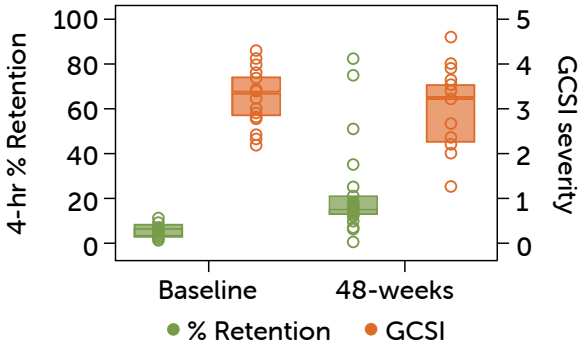
Correlation between delayed gastric emptying and cardinal symptoms are not well established in gastroparesis.[1]

In 2021, a 12-year NIH study of patients with upper GI symptoms found gastric-emptying results are variable and do not correlate with clinical symptoms.[2]



42%

of patients showed emptying improvement without significant improvement in symptoms



37%

of patients showed emptying worsening without significant change in symptoms

Current treatments focused on addressing motility often fail, leaving gastroparesis patients without options focused on relieving nausea and vomiting—the most distressing symptoms of gastroparesis.[3]

Gastroparesis is a quality of life issue

Although it takes an average of 5 years from the onset of symptoms until diagnosis, the journey of gastroparesis hardly ends there — for patients or providers.[3]

Between an evolving understanding of the disease's characteristics and pathophysiology and limited treatment options, gastroparesis remains challenging to treat.

In a recent survey of 1,423 gastroparesis patients, only 4% reported that they were satisfied with available treatment options.[3]

The exhaustion, isolation, and frustration of gastroparesis is real and costly:

68%
Reduction in daily activities[4]

29%
Lower annual income and higher rates of unemployment and underemployment[4]

11%
Medically disabled[4]

24%
Combined anxiety/depression[4]

A different approach to managing gastroparesis

Enterra Therapy is the first and only device designed to reduce the nausea and vomiting secondary to gastroparesis through Gastric Electrical Stimulation (GES).

Implanted in over 15,000 patients, it is an advanced therapy option for gastroparesis patients in their journey to find relief.

Targets nausea & vomiting

Adjustable

Reversible

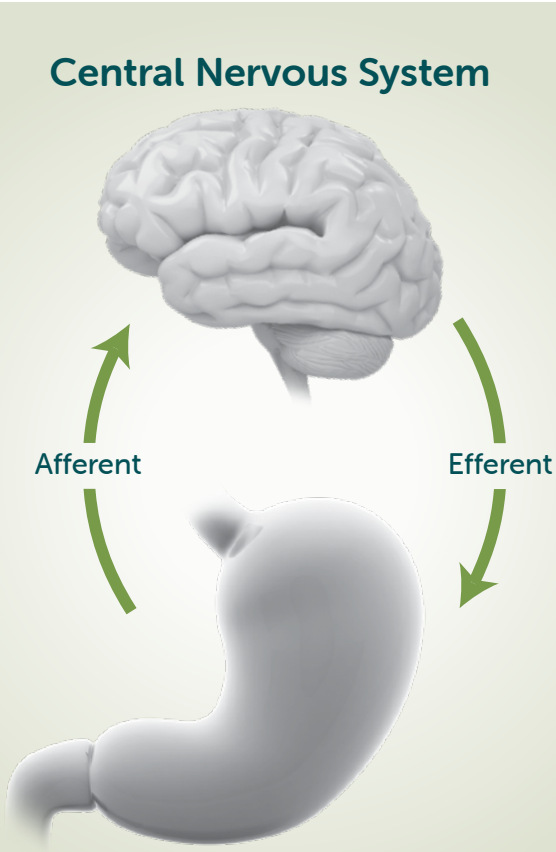
Minimally invasive

Contraindications

The Enterra Therapy System is not intended for patients whom the physician determines are not candidates for surgical procedures and/or anesthesia due to physical or mental health conditions. You cannot have diathermy (deep heat treatment from electromagnetic energy) if you have an Enterra device. Patients should not have Magnetic Resonance Imaging (MRI).

Gastric electrical stimulation: potential mechanism of action

The exact mechanism of action of GES is unknown, but the AGA clinical practice update on the potential mechanism hypothesised that Enterra Therapy may impact the afferent (sensory) and efferent (motor) pathways between the stomach and central nervous system, the cell types found in the circular muscle (ICC-CM), and myoneural connections–allowing for the alleviation of symptoms.[5]



How Enterra Therapy works

Enterra Therapy stimulates the nerves and smooth muscles of the stomach by delivering mild electrical pulses, thereby reducing nausea and vomiting symptoms secondary to gastroparesis.

Neurostimulator

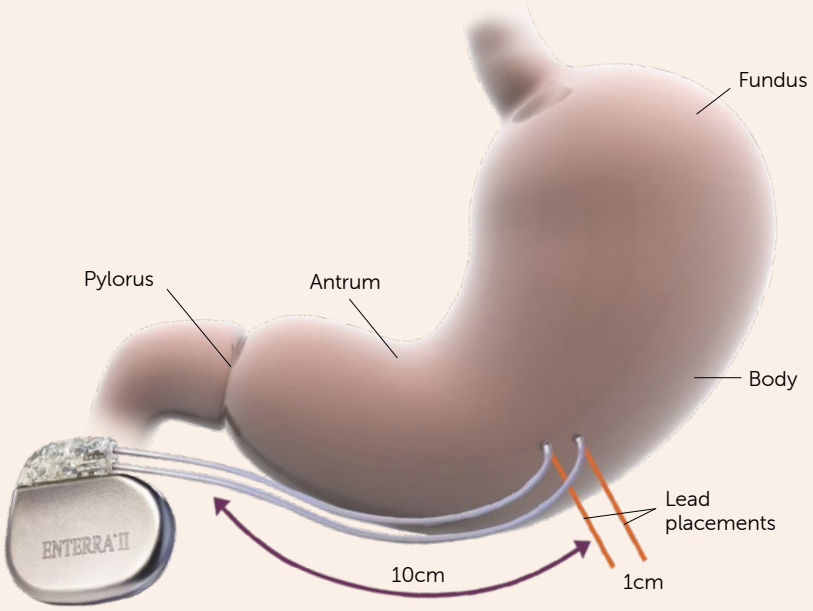
A small, battery-powered gastric neurostimulator is implanted beneath the skin in the lower abdominal region.

Leads

Leads deliver mild, controlled electrical pulses to the antrum portion of the stomach muscle wall.

Programmer

The system is programmed to optimise therapy for the individual patient.



Procedure overview

Electrodes are implanted in the stomach wall

Enterra Therapy implant procedure typically takes 1-2 hours in a minimally-invasive laparoscopic or robotic surgical procedure, where the leads are placed on the serosal surface of the stomach's greater curvature.

Neurostimulator is implanted in subcutaneous abdominal pocket

The neurostimulator is placed in subcutaneous tissue, typically in the abdomen.

Patient recovery is typically 1-2 days

While some patients leave same-day, a 1-2 day hospital stay is typical.

Therapy is adjusted non-invasively

Post-procedure, Enterra Therapy can be adjusted for symptom control via a programmer in an outpatient clinic.

Gastric electrical stimulation is supported by European practice guidelines

Gastroparesis care pathway

Evaluation & Diagnosis

Medical History, Physical Exam	Endoscopy no obstruction	Gastric Emptying Test presence of delayed emptying

First line therapies

Dietary modifications	Pharmacologic Management
• Gastroparesis diet • Glucose control	• Prokinetics • Antiemetics • Cessation of narcotics

Advanced Therapies

Gastric electrical stimulation	Pyloric Surgery	Other treatments
		• feeding tubes • gastrectomy • and more

Adapted from ESNM Consensus

"Current evidence on the efficacy and safety of gastric electrical stimulation for gastroparesis is adequate to support the use of this procedure..."[6]

National Institute for Health and Care Excellence

Studies demonstrate significant improvements in patient symptoms and quality of life

Clinical evidence documenting the results of GES is found in prospective, controlled, multicenter studies.[7,8] Quality of Life (QoL) improvements are from baseline to 12 months.

FRENCH MINISTRY OF HEALTH TRIAL

The largest RCT independently conducted on Enterra Therapy to date.

STATISTICALLY SIGNIFICANT IMPROVEMENT IN **VOMITING FREQUENCY SCORE** DURING THERAPY ON PERIOD VS. OFF PERIOD IN GASTROPARETIC PATIENTS.

(N=133, p=0.01)[9]

U.S. CONTROL TRIAL

SIGNIFICANT REDUCTION IN **MEDIAN WEEKLY VOMITING***

(AT 12 MONTHS)

68%
IMPROVEMENT

DIABETIC GROUP
(N=36, p<0.001)[7]
19.5 TO 4.3 EPISODES

87%
IMPROVEMENT

IDIOPATHIC GROUP
(N=18, p<0.001)[8]
17.3 TO 2.0 EPISODES

SIGNIFICANT REDUCTION IN **HOSPITAL DAYS**

(AT 12 MONTHS)

75%
IMPROVEMENT

DIABETIC GROUP
40 days to 10 days
(N=39, p<0.001)[7]

100%
IMPROVEMENT

IDIOPATHIC GROUP
2 days to 0 days
(N=19, p=0.006)[8]

*The double-blind 3-month period did not show statistically significant reduction in vomiting in the ON vs. OFF period, the primary outcome variable. Manufacturer Sponsored Studies.

A TARGETED APPROACH THAT MAY HELP CONTROL THE SYMPTOMS OF CHRONIC INTRACTABLE NAUSEA AND VOMITING SECONDARY TO GASTROPARESIS.

High patient satisfaction

80%

OVERALL PATIENT SATISFACTION WITH GASTRIC ELECTRICAL STIMULATION AT 10 YEARS[10]

N=37

To learn more about Enterra Therapy talk to your Enterra Medical representative or visit **www.enterramedical.uk**

Enterra Medical is dedicated to helping more people with chronic gastroparesis live better lives through advancing technology, bolstering clinical science, and accelerating patient access to Enterra Therapy.

1. Janssen P, Harris MS, Jones M, et al. The relation between symptom improvement and gastric emptying in the treatment of diabetic and idiopathic gastroparesis. *The American journal of gastroenterology.* 2013;108(9):1382-1391. doi:10.1038/ajg.2013.118.
2. Pasricha, J. et al. Functional Dyspepsia and Gastroparesis in Tertiary Care are Interchangeable Syndromes With Common Clinical and Pathologic Features. *Gastroenterology*. 2021 May; 160(6):2006-2017. doi: 10.1053/j.gastro.2021.01.230.
3. Yu D, Ramsey FV, Norton WF, et al. The Burdens, Concerns, and Quality of Life of Patients with Gastroparesis. *Dig Dis Sci.* 2017;62(4):879-893. doi:10.1007/s10620 017 4456-7.
4. Lacy BE, Crowell MD, Mathis C, Bauer D, Heinberg LJ. Gastroparesis: Quality of Life and Health Care Utilization. *J Clin Gastroenterol.* 2018;52(1):20-244.doi:10.1097/MCG.0000000000000728.
5. Lacy BE, Tack J Gyawali CP, AGA Clinical Practice Updated on Management of Medically Refractory Gastroparesis: Expert Review *Clin Gastroenterol Hepatol.* 2021;S1542-3565(21)01151-4.doi:10.1016/j.cgh.2021.10.038.
6. Gastroelectrical stimulation for gastroparesis. Interventional procedures guidance [IPG489]. www.nice.org.uk/guidance/ipg489. Published: 28 May 2014.
7. McCallum RW, Snape W, Brody F, Wo J, Parkman HP, Nowak T. Gastric electrical stimulation with Enterra Therapy improves symptoms from diabetic gastroparesis in a prospective study. *Clin Gastroenterol Hepatol.* 2010;8:947-954.
8. McCallum RW, Sarosiek I, Parkman HP, Snape W, Brody F, et al. Gastric electrical stimulation with Enterra Therapy improves symptoms of idiopathic gastroparesis. *Neurogastroenterol Motil.* 2013;25(10):815-e636.
9. Ducrotte P, Coffin B, Bonaz B, et al. Gastric Electrical Stimulation Reduces Refractory Vomiting in a Randomized Crossover Trial. Gastroenterology. 2020;158(3):506-514.e2. doi:10.1053/j.gastro.2019.10.018.
10. Hedjoudje A, Huet E, Leroi AM, Desprez C, Melchior C, Gourcerol G. Efficacy of gastric electrical stimulation in intractable nausea and vomiting at 10 years: A retrospective analysis of prospectively collected data. *Neurogastroenterol Motil.* 2020;32(11):e13949. doi:10.1111/nmo.13949.

Important Safety Information
Indications: The Enterra® Therapy System for Gastric Electrical Stimulation (GES) is indicated for the treatment of chronic intractable (drug refractory) nausea and vomiting secondary to gastroparesis. Patients should be carefully selected to assure that their symptoms are of physiological origin. Also, patients must be appropriate candidates for surgery.
Intended clinical benefit: The intended clinical benefit of Enterra Therapy is to reduce chronic intractable (drug refractory) nausea and vomiting secondary to gastroparesis.
Patient selection: Select patients carefully to ensure that: • Their symptoms are of physiological origin. • They are appropriate candidates for surgery.
Contraindications: The Enterra Therapy System is contraindicated in patients whose doctor determines are not candidates for surgical procedures and/or anesthesia due to physical or mental conditions. After implantation of any system component, the following contraindications apply: • Diathermy - Do not use shortwave diathermy, microwave diathermy or therapeutic ultrasound diathermy on patients implanted with a neurostimulation system.
• The Enterra Therapy System is MR unsafe - Patients with an implanted Enterra or Enterra II Therapy System should not be exposed to the electromagnetic fields produced by Magnetic Resonance Imaging (MRI).
• Shelf Life - The Model 37800 IPG must be implanted within 18 months from date of manufacturer. The Model 4351-35 Lead must be implanted within 24 months from date of manufacturer.
Warnings: Use as indicated and instructed - Read all information available for the system. Only use products for the indicated therapy and indicated populations. Bowel obstruction/perforation - The lead can become entangled with or erode into the bowel, which can result in bowel obstruction and perforation. Gastric erosion/perforation - The lead(s) can erode through the stomach wall and result in gastric perforation with possible lead migration into the lumen of the intestine. Patients may experience high lead impedance measurements, decreased therapeutic effect, increased nausea, vomiting, abdominal pain, life threatening intra-abdominal infections and gastrointestinal obstruction that may require laparotomy and/or system revision or removal. Electromagnetic Interference (EMI) – Electromagnetic interference is a field of energy generated by equipment found in the home, work, medical or public environments that is strong enough to interfere with gastric stimulator function. **Precautions:** The safety and effectiveness of this therapy have not been established for: • Pregnancy, unborn fetus, or delivery. • Pediatric use (patients under the age of 18). • Patients over the age of 70. **Adverse events:** Adverse events related to the therapy, device, or procedure can include infection, pain at the surgery site, device components may wear through the skin, bruising at the neurostimulator site, bleeding, loss of therapeutic effect, undesirable change in stimulation (described as a jolting, shocking or burning sensation). The system could stop because of mechanical or electrical problems. Any of these situations may require additional surgery or cause your symptoms to return. For full instructions for use please consult the IFU at https://www.enterramedical.com/intl-hcp/manuals/. For use by healthcare professionals only.

EC REP Authorized Representative
Emergo AR
Westervoortsedijk 60
6827 AT Arnhem
The Netherlands
www.emergobyul.com

CE 0123

www.enterramedical.uk

MKT-B-00942, Rev B

enterra medical®