APOLLO ESG SX™ and APOLLO REVISE SX™

Instructions for Use
Endoscopic Sleeve Gastroplasty (ESG) and Transoral Outlet Reduction (TORe)

Contents

Single use only. Disposable. Do not resterilize.
Caution: Federal law (USA) restricts this device to sale by or on the order of a physician.

Patent Pending.

DISCLAIMER OF WARRANTY AND LIMITATION OF REMEDY

THERE IS NO EXPRESS OR IMPLIED WARRANTY, INCLUDING WITHOUT LIMITATION ANY IMPLIED WARRANTY OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, ON THE APOLLO ENDOSURGERY, INC. PRODUCT(S) DESCRIBED IN THIS PUBLICATION. TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, APOLLO ENDOSURGERY, INC. DISCLAIMS ALL LIABILITY FOR ANY INDIRECT, SPECIAL, INCIDENTAL, OR CONSEQUENTIAL DAMAGES, REGARDLESS OF WHETHER SUCH LIABILITY IS BASED ON CONTRACT, TORT, NEGLIGENCE, STRICT LIABILITY, PRODUCTS LIABILITY OR OTHERWISE. THE SOLE AND ENTIRE MAXIMUM LIABILITY OF APOLLO ENDOSURGERY, INC., FOR ANY REASON, AND BUYER'S SOLE AND EXCLUSIVE REMEDY FOR ANY CAUSE WHATSOEVER, SHALL BE LIMITED TO THE AMOUNT PAID BY THE CUSTOMER FOR THE PARTICULAR ITEMS PURCHASED. NO PERSON HAS THE AUTHORITY TO BIND APOLLO ENDOSURGERY, INC. TO ANY REPRESENTATION OR WARRANTY EXCEPT AS SPECIFICALLY SET FORTH HEREIN. DESCRIPTIONS OR SPECIFICATIONS IN APOLLO ENDOSURGERY, INC PRINTED MATTER, INCLUDING THIS PUBLICATION, ARE MEANT SOLELY TO GENERALLY DESCRIBE THE PRODUCT AT THE TIME OF MANUFACTURE AND DO NOT CONSTITUTE ANY EXPRESS WARRANTIES OR RECOMMENDATIONS FOR USE OF THE PRODUCT IN SPECIFIC CIRCUMSTANCES. APOLLO ENDOSURGERY, INC. EXPRESSLY DISCLAIMS ANY AND ALL LIABILITY, INCLUDING ALL LIABILITY FOR ANY DIRECT, INDIRECT, SPECIAL, INCIDENTAL, OR CONSEQUENTIAL DAMAGES, RESULTING FROM REUSE OF THE PRODUCT.

System Contents and Product Codes

OverStitch Endoscopic Suturing System	ESS-G02-Sx1
OverStitch 2-0 Polypropylene Suture	PLY-G02-020-APL / PLY-G02-020-A
OverStitch Suture Cinch	CNH-G01-000
Tissue Helix	THX-165-028

Caution: Please read all instructions prior to use.

Introduction

The APOLLO ESG SX™ ("APOLLO ESG SX") and APOLLO REVISE SX™ ("APOLLO REVISE SX") devices consist of OverStitch components (suturing instruments, tissue helix, suture-anchors and cinches). APOLLO ESG SX is used to perform endoscopic sleeve gastroplasty (ESG), while APOLLO REVISE SX is intended for revising a previous bariatric surgery through Transoral Outlet Reduction (TORe). The APOLLO ESG SX and APOLLO REVISE SX contain the same types of components, but in different quantities, in order to better accommodate the designated types of procedures.

Physicians performing these procedures should be familiar with endoscopic techniques and proficient with the OverStitch® System. Specific information on how to use the OverStitch components to perform basic suturing and cinching operations is provided in the OverStitch Instructions for Use located at www.apolloendo.com/dfus.

Intended Use

The Apollo ESG SX System is intended to be used by trained gastroenterologists or surgeons that perform bariatric procedures to facilitate weight loss by reducing stomach volume through endoscopic sleeve gastroplasty in adult patients with obesity with BMI between 30-50 kg/m^2 who have not been able to lose weight, or maintain weight loss, through more conservative measures.

The Apollo REVISE SX System is intended to be used by trained gastroenterologists or surgeons that perform bariatric procedures to facilitate weight loss in adult patients with obesity with BMI between 30-50 kg/m^2 by enabling transoral outlet reduction as a revision to a previous bariatric procedure.

Device Description

The APOLLO ESG SX and APOLLO REVISE SX are designed to accomplish endoscopic sleeve gastroplasty (ESG) and Transoral Outlet Reduction (TORe) using a single channel scope. The devices are comprised of the following OverStitch components and the respective quantities of components in the APOLLO ESG SX and APOLLO REVISE SX are shown in Table 1 below. This Instructions for Use documents the use of these devices for specific bariatric indications. Please refer to the Instructions for Use for the OverStitch Sx System (www.apolloendo.com/dfus) for more general information on how to properly operate the OverStitch Sx system, as well as troubleshooting techniques.

Table 1: Component quantities for APOLLO ESG SX and APOLLO REVISE SX devices.

Component	APOLLO ESG SX	APOLLO REVISE SX
OverStitch Sx Handle (ESS-G02-Sx1) to perform suture manipulations.	1	1
Tissue Helix (THX-165-028) to bring tissue into the suturing window.	1	1
Suture-anchors (PLY-G02-020-APL or PLY-G02-020-A, depending on geography) to affect plications.	8	6
Cinch devices (CNH-G01-000) to lock the sutures in place.	8	6

Description of the ESG Procedure

Endoscopic Sleeve Gastroplasty is an endoscopic procedure that involves the creation of plications in the stomach, through a series of stacked suture-based plications, to reduce stomach volume. The plications form a sleeve, which reduces stomach capacity and slows gastric emptying. Over time, there will be scarring and bridging tissue to maintain the reduced gastric volume. Patients receiving ESG should be advised to adopt a healthy lifestyle including proper diet and exercise.

The mechanism of action of ESG is a reduction in stomach volume. Data from a subset of the MERIT Trial patients indicate that ESG is also associated with a delay of gastric emptying, which may alter appetite related regulatory pathways.

In some cases, the plications can fail and come apart. This is most likely to occur with sutures that were not placed "full-thickness" or through sutures breaking over time. This may compromise the effectiveness of the sleeve and patients may report a loss of satiety. In such cases, the sleeve can be revised with new plications or converted to a laparoscopic sleeve gastrectomy, or LSG.

Description of the Bariatric Revision Procedures

Revision procedures are indicated when a patient who undergoes an initial bariatric procedure loses weight, but then reports a loss of satiety, and begins to regain weight. This can be due to dilation of the gastric outlet following gastric bypass or a previous gastric sleeve. Apollo REVISE is used to perform Transoral Outlet Reduction (applying 1 or 2 suture-anchors to reduce the size of the outlet) and is often combined with the placement of 1 to 4 suture-anchors in the stomach to reduce a dilated pouch.

Contraindications

- This system is not for use where endoscopic interventions are contraindicated.
- This system is not for use on malignant tissue.
- Large hiatal hernia.
- Potential bleeding gastric lesions (e.g. ulcers; erosive gastritis; varices; or vascular malformations).
- Affective disorders not under medical supervision or refractory to medical therapy and all eating disorders (e.g. anorexia nervosa; binge eating disorder; specified feeding and eating disorders; avoidant restrictive food intake; rumination).
- Women who are pregnant.
- Coagulopathy and antiplatelet/anticoagulant therapy that cannot be corrected.

Warnings

- Do not use a device where the integrity of the sterile packaging has been compromised or if the device appears damaged.
- Only physicians trained to use OverStitch devices for bariatric procedures should perform the procedures covered in this Instructions for Use.
- Contact of electrosurgical components with other components may result in injury to the patient and/or operator as well as damage to the device and/or endoscope.
- Verify compatibility of endoscopic instruments and accessories and ensure performance is not compromised.
- An overtube device can be used to protect the esophagus. When using an overtube, mount the suturing device onto the scope and verify compatibility with the overtube prior to use. Scope refurbishment may impact compatibility. Thoroughly lubricate the endoscope and overtube prior to use. Never advance or retract the endoscope in an overtube against significant resistance, as this may result in esophageal perforation or laceration.
- Ensure that there is sufficient space in the lumen for the Needle arm to open.
- Ensure that the Handle Grip of the Endoscopic Suturing System is closed and locked during intubation and extubation.
- Reuse or reprocessing of the APOLLO ESG SX or APOLLO REVISE SX components could result in device malfunction or adverse patient consequences, which include:
    - Infection or the transmission of disease;
    - Failure of the handle mechanism causing the device to become locked onto the tissue, which may require surgical intervention;
    - Reduced retention on the endoscope, causing the endcap to detach during use, which may require surgical intervention to retrieve;
    - Reduced retention of the anchor to the needle body, resulting in an inadvertent Anchor drop causing procedural delay or requiring subsequent intervention;
    - Bending of the needle body, preventing the physician from driving the needle correctly or performing the intended procedure; and/or,

    - Failure of the helix to extend fully, limiting the ability to acquire tissue and perform intended procedure.
- If the subject device is used to oversew foreign objects, such as staples, stents, clips, or mesh, it is possible for the needle to become bent, or trapped in the foreign object, requiring surgical intervention for proper removal.
- In situations where the operative site poses a risk of harm to adjacent anatomic structures, use of endoscopic accessories such as the OverStitch Tissue Helix is recommended to retract the tissue intended to be sutured away from these unseen structures.
- It is important to ensure the Tissue Helix is carefully deployed and correctly retracted to avoid entrapping tissue and potentially causing trauma. Avoid using excessive pressure or applying excess turns when deploying the Tissue Helix. Performing more turns than necessary to retract tissue may increase the risk of capturing and suturing an adjacent organ and the risk of the helix entrapping tissue, complicating removal of the instrument.
- Carbon Dioxide (CO_2) is required for insufflation. Room air must not be used to insufflate and could contribute to serious adverse events including pneumoperitoneum, pneumothorax, pneumomediastinum, and death.
- Avoid placing plications in the fundus. The fundus is relatively thin walled and located close to the spleen and diaphragm. Sutures placed in the fundus may increase the risks of leakage and inadvertent suturing of the adjacent organs
- Maintain awareness of the potential to disrupt a short gastric artery along the greater curve. Post procedure pain with any hemodynamic instability should immediately raise concern for extra-gastric bleeding and/or hematoma formation. Management of this should include imaging, e.g. with CT along with serum hemoglobin measurements.
- When cinching the suture anchor to form the plications, use the minimum tension necessary to maintain the plication. Excessive tension may increase the risk of gastrointestinal bleeding or creating a leak. Excessive tension may also increase the risk of the suture-anchor breaking and compromising the gastric sleeve.
- Patients who develop significant persistent upper abdominal pain at any time after an ESG, with radiation to the back or supraclavicular area along with pleuritic symptoms or even dyspnea, may have developed a needle puncture site leak with the development of a sterile or infected fluid collection and inflammatory pleural effusion. These symptoms warrant investigation with an imaging study, e.g. CT.

Precautions

- The System may only be used if purchased from Apollo Endosurgery, Inc. or one of its authorized agents.
- Placing the patient in a supine to modified (semi supine) left lateral decubitus position, creates additional safety margin between the stomach and surrounding structures.
- Take care when using plasma coagulation marking. Perforation could occur while using plasma coagulation and/or coagulated tissue may slough off later, resulting in delayed gastrointestinal bleeding.
- The Tissue Helix must be kept clean from debris during use; this may require periodic debridement of the helix coil during use.
- During a revision procedure, the physician should carefully consider the specific anatomy being revised and the presence of previous devices that may have been placed during the original procedure.

System Compatibility

The APOLLO ESG SX and APOLLO REVISE SX devices are compatible with single channel endoscopes having an insertion tube and distal diameter between 8.3 mm and 9.8 mm, a working length of up to 110 cm, and using overtubes having an inner diameter of at least 16.7 mm. As scope dimensions can be affected by refurbishment, verify compatibility prior to the procedure.

Adverse Events

Adverse events are generally ordered by decreasing anticipated frequency.

- Pharyngitis / Sore throat
- Vomiting
- Nausea
- Moderate abdominal pain more than 24 hours after procedure. In some cases, abdominal pain may be severe and require medical intervention
- Constipation
- Generalized weakness after procedure
- Heartburn
- Fever
- Gastrointestinal bleeding (with or without melena or hematemesis)
- Pharyngitis / Sore throat
- Vomiting
- Dehydration and/or nutritional deficiency requiring hospital admission
- Perigastric fluid collection
- Leak
- Hemoperitoneum
- Hematoma
- Paresthesia
- GERD
- Peritonitis
- Pneumoperitoneum
- Pulmonary Embolism
- Perforation (gastric or esophageal)
- Pneumothorax
- Pneumomediastinum
- Gall bladder suture
- Spleen Laceration
- Deep Vein Thrombosis
- Esophageal tear
- Pleural effusion
- Persistent Vomiting
- Bowel obstruction
- Infection/sepsis
- Bloating
- Stricture
- Liver abscess
- Intra-abdominal (hollow or solid) visceral injury
- Aspiration
- Shortness of breath
- Acute inflammatory tissue reaction
- Death

NOTE: Any serious incident that has occurred in relation to the APOLLO ESG SX or APOLLO REVISE SX should be reported to Apollo Endosurgery (see contact information at the end of this document) and any appropriate government entity.

Materials

Cinch implants are manufactured from polyetheretherketone (PEEK).

Suture-Anchor Materials:

The suture is manufactured from an isotactic crystalline stereoisomer of polypropylene, a synthetic linear polyolefin. The suture pigment uses CU-Phthalocyanine Blue Dye (<0.5 WT %) to enhance visibility. The suture material meets the requirements established by USP.

The suture anchor is manufactured from cobalt chromium and stainless-steel alloys (anchor tip: cobalt chromium steel (MP35N; anchor body: 316L stainless steel).

The suture-anchor materials have been subject to a toxicological risk assessment that supports the use of up to eight suture-anchors in a single patient.

The APOLLO ESG SX and Apollo REVISE SX devices, including the implants and delivery system, are not made from natural rubber latex.

All implants and patient contacting delivery instruments have been tested and evaluated in accordance with appropriate ISO-10993 standards for suitable biocompatibility.

CMR-ED Statement – Some of the metal components within this device contain the following substance(s) defined as carcinogenic, mutagenic or toxic to reproduction (CMR) 1A/1B and/or endocrine disrupting (ED) in a concentration above 0.1% weight by weight: Cobalt (CAS No. 7740-48-8; EC No. 231-158-0).

Current scientific evidence supports that medical devices manufactured from these cobalt alloys, or stainless steels containing cobalt, do not cause increased risk of cancer or adverse reproductive effects.

Clinical Evaluation of ESG (MERIT Trial)

Study Purpose

The Multi-center ESG Randomized Interventional Trial (MERIT-Trial) evaluated the effectiveness and safety of ESG as an adjunct to life-style intervention for weight loss and improvement in obesity-related comorbidities compared to lifestyle intervention alone, in participants 21-65 years of age with BMI ≥30 and ≤40 kg/m² and who have failed to achieve and maintain weight loss with a non-surgical program. The study aimed to enroll up to 200 subjects (80 ESG and 120 controls) and to enroll at least 50 patients with hypertension, at least 50 with Type II diabetes mellitus (T2DM), and to enroll no more than 50 patients with no weight-related comorbidities.

Study Design

This was a prospective, randomized, multicenter study and subjects were followed for two years. Patients were randomized in a 1:1.5 ratio of treatment (ESG + lifestyle modification) to controls (lifestyle modification). At one year, patients in the control group were allowed to cross-over to ESG if they had not responded to lifestyle modification (defined as not having achieved ≥25% Excess Weight Loss (EWL)) and had completed their follow-up visits.

Study Population

There were 85 Treatment and 124 Control subjects randomized. Eight subjects in the Treatment group did not receive treatment and were removed from the study. Twelve subjects in the Control group did not complete a single visit and 2 additional Control subjects were determined to be ineligible prior to starting the study. As a result, 77 Treatment and 110 Control subjects received the assigned treatment. Of these, 55 and 113 had baseline comorbidities of Type II Diabetes or hypertension, respectively, defined as a having a pre-existing diagnosis from their primary care physician and currently taking medications specifically for that comorbidity. Of those, 37 subjects had both baseline diagnosis of both diabetes and hypertension. Three Treatment subjects withdrew consent prior to the 52 week visit and six were lost to follow-up. In the Control group, 13 withdrew consent and eight were lost to follow-up prior to completing the 52 week visit. As a result, there were 68 Treatment and 89 Control subjects with effectiveness data at 52 weeks. Of the subjects with data at 52 weeks; 45 and 92 subjects had baseline comorbidities of Type II diabetes and hypertension, respectively.

Data Source

This multicenter study was sponsored by the MAYO Clinic (Rochester, MN) and financial support was provided by Apollo Endosurgery, Inc. as part of a collaborative research agreement. Institutional Review Board (IRB) approval was obtained by all sites prior to enrolling subjects for the study. The study data were compiled by the MAYO Clinic, provided to Apollo Endosurgery for independent analysis, and submitted for FDA review.

Key Study Endpoints

The primary effectiveness endpoint of Apollo's analysis was to assess the responder rate, defined as at least 10% Total Body Weight Loss (%TBWL), at 52 weeks. The %TBWL was derived at each post-placement study visit for each subject where a weight measurement was collected. The primary effectiveness endpoint was summarized for the effectiveness population and included 95% confidence intervals. Secondary effectiveness endpoints collected as part of the investigational plan included %Excess Weight Loss (EWL) and change in BMI from baseline. Along with %TBWL, these data were collected at each visit and used to evaluate the effectiveness of Treatment and Control, retightening of an ESG, and crossing over from lifestyle modification to ESG, over time.

All adverse events were recorded. Serious adverse events (defined as a death, a life-threatening event, or hospitalization of at least 24 hours), and select adverse events deemed notable by the clinical sites, were reviewed by an independent Data Monitoring Committee and categorized using the Clavien-Dindo classification. Adverse events graded as Clavien-Dindo Class III or higher were identified for reporting as safety failures. The primary safety endpoint was the percentage of adverse events with Clavien-Dindo Grade III or higher, including a one-sided confidence interval.

Analysis Population

The population for the effectiveness analysis was the mITT population, which included all eligible subjects regardless of adherence to follow-up visits or the treatment program. The mITT population was defined as follows:

- Subjects in both groups that met the eligibility criteria for the study.
    - Treatment group subjects that had an EGD with confirmation of satisfying anatomical and medical criteria and completed the ESG were included in the mITT.
    - Treatment and Control group subjects that were confirmed ineligible based upon baseline visit information, were excluded from study analysis, even if the subject completed study visits prior to exclusion.
- Subjects in the Control group that completed at least one follow-up visit following randomization.

The population for the safety analysis included all mITT patients that were assigned to have an ESG procedure, either as randomized or as a cross-over from lifestyle intervention alone to the ESG group.

Total Number of Enrolled Subjects and Patient Demographics

Nine sites enrolled a total of 187 subjects that made up the modified Intent to Treat (mITT) population. See Table 2 below for details on sample sizes and demographics at enrollment. There were 157 subjects that completed the study through 52 weeks.

Table 2: Demographics for mITT Population by Randomized Treatment Group

Description	Control (Lifestyle Modification)	Treatment (ESG + Lifestyle Modification)	p-value
N	110	77	
Weight (kg)			
Mean ± StdDev	99.2 ± 12.775	98.1 ± 12.346	0.641
Median	97.5	95.3	
Min, Max	73.8, 138.7	74.4, 130.0	
95% CI	96.7, 101.6	95.3, 100.9	
BMI (kg/m^2)			
Mean ± StdDev	35.74 ± 2.6167	35.37 ± 2.5654	0.357
Median	35.78	35.52	
Min, Max	30.12, 39.88	31.01, 39.83	
95% CI	35.25, 36.24	34.79, 35.96	
Age (years)			
Mean ± StdDev	45.7 ± 10.072	47.3 ± 9.323	0.269
Median	45.5	49.0	
Min, Max	23, 65	22, 64	
95% CI	43.8, 47.6	45.22, 49.45	
Gender			
Male	17 (15.5%)	9 (11.7%)	0.525
Female	93 (84.5%)	68 (88.3%)	

Race			
White	62 (56.4%)	53 (68.8%)	0.136
African American	14 (12.7%)	11 (14.3%)	
Asian	3 (2.7%)	0 (0.0%)	
Hispanic / Latino	18 (16.4%)	11 (14.3%)	
Other	9 (8.2%)	1 (1.3%)	
Deferred	4 (3.6%)	1 (1.3%)	
Weight Related Comorbidities*			
Type II Diabetes	36 (32.7%)	19 (24.7%)	0.234
Hypertension	72 (65.5%)	41 (53.2%)	0.931

*For Apollo's analysis, the assignment to Type II diabetes and/or hypertension was based on an existing diagnosis from the patient's primary healthcare provider combined with taking medication specifically for that diagnosis. Subjects could be identified as having both type II diabetes and hypertension.

Study Visits and Follow-Up Rates

Visits reported in this study were baseline, 1 week, 4 week, 8 weeks, 12 weeks, 24 weeks, and 52 weeks for the initial randomization groups (Treatment and Control). Additional visits for the Treatment group were at 60 weeks, 72 to 76 weeks and 104 weeks. Control subjects were then allowed to cross-over to ESG. Controls were then followed for 52 weeks following crossover to ESG, in the same schedule as the initial randomization of the Treatment group (1, 4, 8, 12, 24 and 52 weeks after crossover).

The follow-up rates are provided for Control and Treatment groups in Table 3 and Table 4, respectively.

Table 3: Accountability by Follow-up Visit, Primary Endpoint: Control Subjects

	1 week	**4 week**	**8 week**	**12 week**	**24 week**	**52 week**
Theoretical #	110	110	110	110	110	110
Withdrawn		2	6	6	8	13
Lost to Follow-up			1	2	5	8
Expected*	110	108	104	104	102	97
Visit Weight Data	103	92	90	89	85	89@
Missed Visit	7	16	13	13	11	0
% Follow-up – Effectiveness Data^	93.6%	84.3%	86.5%	85.6%	83.3%	91.8%

Subjects in the mITT population
* Expected = Theoretical – Withdrawn
^ % Follow-up = Visit Weight Data / Expected *100
@ Theoretical subjects for cross-over portion of the study

Table 4: Accountability by Follow-up Visit, Primary Endpoint: Treatment Subjects

	1 week	**4 week**	**8 week**	**12 week**	**24 week**	**52 week**
Theoretical #	77	77	77	77	77	77
Withdrawn					1	3
Lost to Follow-up						6
Expected*	77	77	77	77	76	74
Visit Weight Data	76	72	70	62	70	68@
Missed Visit	1	5	7	15	6	0

% Follow-up – Effectiveness Data^	98.7%	93.5%	90.9%	79.2%	92.1%	91.9%

Subjects in the mITT population
* Expected = Theoretical – Withdrawn
^ % Follow-up = Visit Weight Data / Expected *100
@ Theoretical subjects for 52-104 months of the study. One additional subject had known safety information available

Due to the Covid-19 pandemic, starting in March 2020, accommodations were made to permit self-reported weight measurements. Based on an analysis by Apollo Endosurgery, it is estimated that 10% and 13% of the weight measurements at 52 weeks were self-reported, in the Control and Treatment groups, respectively. Previous visits were not impacted. Nine percent of visits 52 weeks after cross-over are likely to have been self-reported. Earlier visits, following cross-over, may have had as high as 40% of the weight related measurements self-reported. This reflects the timing of the most stringent pandemic lock down conditions at the study site locations.

Final Effectiveness Findings

The primary effectiveness analysis is reported in Table 5. Responder rates at 52 weeks, as defined by achieving ≥10 %TBWL, in the completers population were 64.7% and 4.5% in Treatment and Control groups, respectively. Sensitivity analysis, including Last Observation Carried Forward , and Best and Worst Case Scenarios for missing data imputation, all showed a higher responder rate in the Treatment group compared to Control group.

Table 5: Responder rates at 52 weeks, based on achievement of 10%TBWL in the mITT population.

Population	Control	Treatment	Difference	Standard Error of Difference	95% CI*	p-value
Completers Rate CI (95%)	 4/89 (4.5%) 1.2, 11.1	 44/68 (64.7%) 52.2, 75.9	-60.2	6.2	-71.0, -46.6	<0.001
LOCF[#] Rate CI (95%)	 5/110 (4.5%) 1.5, 10.3	 48/77 (62.3%) 50.6, 73.1	-57.8	5.9	-68.2, -45.2	<0.001
Best Case Scenario[#] Rate CI (95%)	 25/110 (22.7%) 15.3, 31.7	 53/77 (68.8%) 57.3, 78.9	-46.1	6.6	-58.0, -32.2	<0.001
Worst Case Scenario[#] Rate CI (95%)	 25/110 (22.7%) 15.3, 31.7	 44/77 (57.1%) 45.4, 68.4	-34.4	6.9	-47.2, -20.3	<0.001

[#] LOCF = last observation carried forward. Best case was calculated assuming that all Treatment and Control subjects lost to follow up were responders. Worst case scenario was that all Treatment subjects lost to follow-up were non-responders but all control subjects lost to follow-up were responders.
* Confidence interval was obtained based on the Agresti-Caffo confidence interval method, without multiplicity adjustment made.

Additional analyses were performed to report responder rates at 52 weeks (10%TBWL) by various subgroups. Table 6 below shows that responder rates across the subgroups defined by age, gender, race, BMI, type II diabetes, and hypertension at baseline in the completers population were all higher in the Treatment group than in the Control group.

Table 6: Sub-group responder rates at 52 weeks based on achievement of at least 10%TBWL in the Completers population.

Comparison	Sub-Group	Control	Treatment	Difference	Standard Error of Difference	95% CI
Age	< 50 years	3/66 (4.5%)	22/37 (59.5%)	-54.9	8.5	-69.5, -36.7
	≥ 50 years	1/23 (4.3%)	22/31 (71.0%)	-66.6	9.2	-80.6, -42.8
Gender	Male	0/11 (0%)	6/9 (66.7%)	-66.7	15.7	-87.8, -24.0
	Female	4/78 (5.1%)	38/59 (64.4%)	-59.3	6.7	-70.9, -44.5
BMI	<35 kg/m^2	3/41 (7.3%)	24/31 (77.4%)	-70.1	8.5	-83.5, -49.5
	≥ 35 kg/m^2	1/48 (2.1%)	20/37 (54.1%)	-52.0	8.4	-66.4, -33.3
Race	Caucasian	3/51 (5.9%)	34/47 (72.3%)	-66.5	7.3	-78.4, -49.4
	Non-Caucasian	1/38 (2.6%)	10/21 (47.6%)	-45.0	11.2	-64.3, -21.3
Type II Diabetes	Yes	0/27 (0%)	11/18 (61.1%)	-61.1	11.5	-79.0, -34.1
	No	4/62 (6.5%)	33/50 (66.0%)	-59.5	7.4	-72.1, -43.1
Hypertension	Yes	1/55 (1.8%)	22/37 (59.5%)	-57.6	8.3	-71.6, -39.3
	No	3/34 (8.8%)	22/31 (71.0%)	-62.1	9.5	-77.3, -39.8

* Confidence interval was obtained based on the Agresti-Caffo confidence interval method, without multiplicity adjustment made.

The mean %TBWL is shown for each follow up visit in Table 7. Subjects in the Treatment group began to lose weight as early as the one week visit. Weight loss steadily progressed through 24 weeks (14.70, SD 5.62 %TBWL) then plateaued, with minimal weight regain at 52 weeks (13.86, SD 8.06 %TBWL). Comparatively, subjects in the Control group experienced very little weight loss through 52 weeks (0.76, SD 4.97 %TBWL).

Table 7: %TBWL by Randomized Group and Visit for the mITT Population

Weeks	Descriptive	Control	Treatment	Difference*
1	Mean ± StdDev	0.43 ± 1.7946	-5.08 ± 3.9745	5.51 ± 0.4890
	N	103	76	
	Median	0.11	-4.61	
	Min, Max	-4.94, 4.89	-29.00, 1.89	
	95% CI	0.08, 0.78	-5.99, -4.17	4.54, 6.48
4	Mean ± StdDev	-0.08 ± 2.2065	-8.47 ± 3.9968	8.39 ± 0.5242
	N	92	72	
	Median	0.00	-8.03	
	Min, Max	-7.79, 5.86	-33.36, -1.32	
	95% CI	-0.54, 0.37	-9.41, -7.53	7.35, 9.43
8	Mean ± StdDev	-0.42 ± 2.7118	-11.09 ± 4.4888	10.67 ± 0.6079
	N	90	70	
	Median	-0.17	-10.96	
	Min, Max	-7.32, 6.06	-35.36, -3.64	
	95% CI	-0.99, 0.15	-12.16, -10.02	9.47, 11.88
12	Mean ± StdDev	-0.94 ± 3.1050	-13.14 ± 4.9838	12.21 ± 0.6588
	N	89	62	
	Median	-0.55	-11.83	
	Min, Max	-8.81, 4.44	-37.18, -3.88	
	95% CI	-1.59, -0.28	-14.41, -11.88	10.79, 13.62
24	Mean ± StdDev	-1.36 ± 4.5586	-14.70 ± 5.6167	13.34 ± 0.8172

Weeks	Descriptive	Control	Treatment	Difference*
	N	85	70	
	Median	-0.80	-13.51	
	Min, Max	-14.31, 7.49	-29.03, 0.36	
	95% CI	-2.34, -0.38	-16.04, -13.36	11.73, 14.96
52	Mean ± StdDev	-0.76 ± 4.9711	-13.86 ± 8.0585	13.10 ± 1.1102
	N	89	68	
	Median	-0.39	-12.88	
	Min, Max	-17.62, 9.91	-40.91, 6.84	
	95% CI	-1.81, 0.29	-15.81, -11.91	10.89, 15.30
60	Mean ± StdDev	NA	-14.72 ± 7.9433	NA
	N		57	
	Median		-13.66	
	Min, Max		-34.09, 1.08	
	95% CI		-16.82, -12.61	
72-76	Mean ± StdDev	NA	-13.93 ± 7.4285	NA
	N		61	
	Median		-12.40	
	Min, Max		-37.00, 0.05	
	95% CI		-15.84, -12.03	
104	Mean ± StdDev	NA	-12.20 ± 8.5461	NA
	N		59	
	Median		-11.29	
	Min, Max		-34.91, 8.13	
	95% CI		-14.43, -9.97	

* Difference = Control – Treatment and 95% CIs are not adjusted for multiplicity.

The mITT populations also observed the same type of changes in %EWL and changes in BMI. At the 52 week visit, Treatment and Control subjects reported a loss of 49.81 (SD, 31.40) and 2.98 (SD, 17.97) %EWL, respectively. Similarly, BMI in Treatment and Control subjects reduced by 4.76 (SD, 2.57) and 0.26 (SD, 1.77) kg/m^2, respectively, at 52 weeks.

Table 8 presents the %TBWL at each follow up visit in patients that were assigned to the Control group but crossed over to the Treatment group at 52 weeks. As early as the 1 week visit, subjects that crossed over to ESG lost more weight than they had with lifestyle modification. Weight loss steadily progressed through 24 weeks then plateaued, with minimal weight regain at 52 weeks. This was the same pattern demonstrated by subjects randomized to ESG. After 52 weeks of lifestyle modification alone, these crossover subjects lost 0.18 (SD, 4.47) %TBWL. Then, 52 weeks after crossing over to ESG, these same subjects had lost 12.95 (SD, 8.64) %TBWL.

Table 8: %TBWL: Control and Cross-Over

Weeks	Description	Control	Cross-Over	Difference*
1	Mean ± StdDev	0.38 ± 1.494	-4.38 ± 2.165	4.75 ± 0.315
	N	67	71	
	Median	0.24	-4.32	
	Min, Max	-3.89, 4.89	-10.27, 0.50	
	95% CI	0.01, 0.74	-4.89, -3.87	4.13, 5.38
4	Mean ± StdDev	0.12 ± 1.820	-7.70 ± 2.978	7.82 ± 0.423
	N	63	70	
	Median	0.00	-7.38	
	Min, Max	-4.37, 4.78	-16.05, 6.43	

	95% CI	-0.34, 0.57	-8.41, -6.99	6.98, 8.66
8	Mean ± StdDev	-0.34 ± 2.518	-10.35 ± 2.855	10.74 ± 0.610
	N	64	68	
	Median	-0.55	-10.45	
	Min, Max	-6.49, 5.09	-17.68, -4.05	
	95% CI	-0.97, 0.29	-11.04, -9.66	9.07, 10.93
12	Mean ± StdDev	-0.77 ± 2.936	-11.50 ± 4.097	10.91 ± 4.786
	N	67	69	
	Median	-0.55	-10.29	
	Min, Max	-8.58, 4.44	-28.77, -4.27	
	95% CI	-1.48, -0.05	-12.49, -10.52	9.53, 11.94
24	Mean ± StdDev	-0.69 ± 3.910	-13.35 ± 5.77	12.66 ± 0.849
	N	64	69	
	Median	-0.14	-12.28	
	Min, Max	-12.97, 7.49	-32.36, -3.83	
	95% CI	-1.67, 0.28	-14.74, -11.97	10.98, 14.34
52	Mean ± StdDev	-0.18 ± 4.473	-12.95 ± 8.636	12.77 ± 1.242
	N	72	59	
	Median	-0.02	-12.17	
	Min, Max	-17.62, 7.11	-36.64, 4.09	
	95% CI	-1.23, 0.87	-15.20, -10.70	10.30, 15.24

* Difference = Control – Treatment and 95% CIs are not adjusted for multiplicity.

The cross-over population also demonstrated the same type of changes in %EWL and changes in BMI. At the 52 week visit after cross-over, subjects reported a loss of 46.85 (SD, 37.97) compared to 0.44 (SD, 15.34) %EWL over the 52 weeks of lifestyle modification prior to crossing over. Similarly, BMI reduced by 4.59 (SD, 2.10) 52 weeks after crossing over, compared to a reduction of just 0.07 (SD, 1.61) kg/m^2, after the 52 weeks of lifestyle modification prior to crossing over. The weight loss from subjects following crossover was consistent with the amount of weight loss in subjects randomized to the Treatment group.

Retightening of ESG

Fourteen ESG patients had a secondary procedure to retighten the original ESG procedure. At 52 weeks prior to the retightening procedure, mean weight loss was 3.84 (SD, 4.31) %TBWL in 9 subjects that had not experienced at least 25% EWL, and 10.94 (SD, 3.02) %TBWL in 5 subjects that had lost more than 25% EWL. This is compared to 15.8 (SD, 7.5) %TBWL in the 54 Treatment subjects still under study at 52 weeks that were not retightened. At 104 weeks, 52 weeks after retightening, the mean weight loss from baseline (index ESG procedure) was 7.10 (SD, 5.1) %TBWL in the < 25% EWL group (9 subjects) and 11.6 (SD, 7.6) %TBWL in the > 25% EWL group (5 subjects). Similarly, %EWL and change in BMI were greater for the subjects with >25% EWL prior to the retightening procedure. No adverse events were associated with the retightening procedure. If retightening is performed, subjects may demonstrate weight maintenance or modest incremental weight loss following the retightening procedure. Retightening of the ESG has the same adverse event profile as the primary ESG procedure.

Final Safety Findings

The safety population includes subjects from both the initial ESG group and cross-over ESG group for a total of 150 subjects. Of these 150 subjects, 146 and 131 subjects had complete safety data through 24 and 52 weeks since the ESG, respectively. The observed rate of device or procedure related, Clavien-Dindo Grade III or higher, events was 2.3% (3/131) and the upper limit of the 1-sided 95% confidence interval was 6.5%. Table 9 summarizes the primary safety endpoint analysis and imputations associated with the study.

Table 9: Primary Safety Endpoint: Incidence of Device and/or Procedure Related, Clavien-Dindo Grade III or higher, through 52 Weeks.

Analysis Population	Weeks	SAE Incidence Rate	Upper Limit of 1-sided 95% CI
Completers	52	3 / 131 (2.3%)	6.5%
Imputation (Best Case)	52	3 / 150 (2.0%)	5.7%
Imputation (Worst Case)^	52	22 / 150 (14.7%)	21.4%

^ Worst case scenario assumed that subjects with missing data had a safety endpoint event. Subjects that continue in active follow-up and have completed their 24-week visit were not reported as an SAE in Worst Case as all reported SAEs occurred prior to the 12 week visit. This ensures that subjects that continue to be followed but are not yet due for their expected visits to not negatively impact the imputation.

* Confidence interval was obtained based on the Agresti-Caffo confidence interval method, without multiplicity adjustment made.

The three adverse events rated Clavien-Dindo Grade III or higher were as follows. One patient presented with an abdominal abscess and plural effusion two weeks after ESG. One patient was admitted at 11 weeks following ESG with weakness, dehydration, altered mental status and was suspected of malnutrition. This case was treated by endoscopically cutting sutures to open the sleeve. One patient was kept in the hospital after the ESG due to abdominal pain, nausea and vomiting. It was determined that this patient had bleeding associated with the use of Argon Plasma Coagulation to mark the intended suture locations. Upon follow-up EGD, this patient was found to have an amount of clotted blood, which was located in the cardia (between the stomach and esophagus). All three cases resolved with medical intervention.

An additional safety analysis was performed using FDA's traditional definition of a Serious Adverse Event (SAE). There were 21 device or procedure related SAEs reported from 11 of the 150 subjects receiving ESG (including primary and cross-over subjects). This represents an SAE rate of 7.3% (11/150; 95% CI: 3.7-12.7%) See Table 10. The most frequently reported SAEs were nausea, abdominal pain and vomiting. The FDA definition resulted in a higher SAE rate because the investigational plan aimed to discharge patients the day of the procedure, and 7 patients were hospitalized to address early post-operative symptoms associated with accommodation to the sleeve, primarily nausea and vomiting. Treatments consisted of IV fluids, pain medications and anti-emetics and all adverse events resolved prior to discharge. There was also a device related adverse event that resulted in a mucosal tear in the esophagus. The decision was made not to complete the procedure. The patient was kept in the hospital for three days and then discharged.

Table 10: Overview of Device and/or Procedure Related Serious Adverse Events by Subject

Serious Adverse Event[1]	# Subjects (% Subjects)	# Events	Onset (days to event)
Abdominal Abscess	1/150 (0.7%)	1	15
Abdominal Pain	3/150 (2.0%)	3	Mean = 1.7 Median = 2 Range = 0-3
Bloody Stools	1/150 (0.7%)	1	0
Bowel Impaction	1/150 (0.7%)	1	81
Dehydration	1/150 (0.7%)	1	5
Esophageal Mucosal Tear	1/150 (0.7%)	1	0
GI bleeding at Argon Plasma Coagulation site	1/150 (0.7%)	1	0
Malnutrition[2]	1/150 (0.7%)	1	77
Nausea	5/150 (3.3%)	5	Mean = 0.8 Median = 1 Range = 0-2
Pleural Effusion	1/150 (0.7%)	1	20
Pneumonitis	1/150 (0.7%)	1	4

Sore Throat	1/150 (0.7%)	1	8
Vomiting	3/150 (2.0%)	3	Mean = 0.3 Median = 0 Range = 0-1
Total	11/150 (7.3%)	21	Mean = 11 Median = 2 Range = 0-81

[1] A serious adverse event is one that:

- Led to death
- Resulted in serious deterioration in the health of the subjects that results in:
  - Life-threatening illness or injury
  - Permanent impairment of a body structure or a body function
  - The need for in-patient care or prolongation of hospitalization (this does not include the optional 23 hours observation admission after ESG or re-tightening procedure)
  - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
- Planned hospitalization for a pre-existing condition, or a procedure required by the trial protocol, without serious deterioration in health, is not considered a serious adverse event

[2] This patient was treated by endoscopically cutting sutures to open the sleeve.

Considering gastrointestinal adverse events that could be attributed to the device or procedure, the most common events were nausea, abdominal pain, constipation, eructation, constipation, heartburn and diarrhea. See Table 11. All of these types of events tended to initiate within the first week of the procedure and to resolve within 30-60 days.

Table 11: All Gastrointestinal Device and/or Procedure Related Adverse Events Occurring in > 10% of Subjects

Adverse Event	Number of Subjects (% subjects) N=150	Date of Onset: Median (Mean) Range	Duration in Days[1]: Median (Mean) Range	Severity[2] n/N (%): Mild[3] Moderate[4] Severe[5] Unknown[6]	# Subjects with onset <= 3 days post-procedure (% Subjects)	# Subjects with onset <= 3 post-procedure with duration > 14 days and <= 30 days (% Subjects)	# Subjects with onset <= day 3 post-procedure with duration > 30 days (% Subjects)
Abdominal Pain[7]	102 (68.0%)	0 (37.5) 0-704	4 (16.1) 1-162	77/102 (75.5%) 22/102 (21.6%) 3/102 (2.9%) 0/102 (0%)	82/102 (80.4%)	8/82 (9.8%)	6/82 (7.3%)
Constipation[7]	68 (45.3%)	7 39.5 0-567	26 51.5 1-368	51/68 (75.0%) 17/68 (25.0%) 0/68 (0%) 0/68 (0%)	30/68 (44.1%)	3/30 (10.0%)	12/30 (40.0%)
Diarrhea[7]	23 (15.3%)	8 65.3 0-427	8 25.7 1-296	20/23 (87.0%) 2/23 (8.7%) 0/23 (0%) 1/23 (4.3%)	9/23 (39.1%)	1/9 (11.1%)	1/9 (11.1%)
Eructation[7]	77 (51.3%)	1 19.1 0-366	27 45.8 1-403	67/77 (87.0%) 10/77 (13.0%) 0/77 (0%) 0/77 (0%)	55/77 (71.4%)	5/55 (9.1%)	24/55 (43.6%)
Heartburn / Reflux	55 (36.7%)	2 40.1 0-550	10 44.5 1-253	40/55 (72.7%) 14/55 (25.5%) 0/55 (0%) 1/55 (1.8%)	34/55 (61.8%)	4/34 (11.8%)	9/34 (26.5%)

Nausea	105 (70.0%)	0 9.5 0-365	3 7.7 1-89	76/105 (72.4%) 24/105 (22.8%) 5/105 (4.8%)	92/105 (87.6%)	3/92 (3.3%)	3/93 (3.3%)
Vomiting	74 (49.3%)	0 23.5 0-541	2 8.1 1-368	54/74 (73.0%) 16/74 (21.6%) 3/74 (4.1%) 1/74 (1.3%)	60/74 (81.1%)	0/60 (0%)	1/60 (1.7%)

[1] Duration in Days = Date of Resolution – Date of Onset +1. Thus, an event that resolved the same day as onset will have a day of resolution = 1.
[2] Subjects with multiple events of the same type are reported by first occurrence with the highest severity
[3] Mild = awareness of sign or symptom, but easily tolerated, although not specifically defined in the study protocol
[4] Moderate = discomfort enough to cause interference with usual activity, although not specifically defined in the study protocol
[5] Severe = incapacitating with inability to work or do usual activity, although not specifically defined in the study protocol
[6] Unknown = no response was recorded in the electronic database.
[7] The following events did not have a resolution date recorded and were excluded from the duration calculations (1 report of Abdominal pain, 3 reports of constipation, 1 report of diarrhea, and 1 report of eructation).

There were 935 device or procedure related adverse events reported in the study. See Table 12. Of the 150 subjects that had an ESG (including primary and cross over subjects), 138 (92%) experienced at least one device or procedure related adverse event and 132 (88%) experienced at least two. Some subjects reported multiple instances of a given type of adverse event. These types of adverse events were most likely to be abdominal pain, eructation, constipation, and nausea.

Table 12: All Device and/or Procedure Related Adverse Events

Adverse Event[1]	# Subjects[2] with Events (% Subjects)	# Events[3] (% Events)	# Subjects with Event Occurrence > 1 (% Subjects)
Abdominal Abscess	1 (0.7%)	1 (0.1%)	0 (0%)
Abdominal Pain	102 (68.0%)	143 (15.3%)	28 (18.7%)
Abdominal Spasm	1 (0.7%)	1 (0.1%)	0 (0%)
Back Pain	1 (0.7%)	1 (0.1%)	0 (0%)
Bloody Stools	8 (5.3%)	10 (1.1%)	2 (1.3%)
Blurred Vision	1 (0.7%)	1 (0.1%)	0 (0%)
Bowel Impaction	1 (0.7%)	1 (0.1%)	0 (0%)
Burning	1 (0.7%)	1 (0.1%)	0 (0%)
Chest Pain	1 (0.7%)	1 (0.1%)	0 (0%)
Chills	1 (0.7%)	1 (0.1%)	0 (0%)
Concentrated Urine	22 (14.7%)	28 (3.0%)	3 (2.0%)
Constipation	68 (45.3%)	102 (10.9%)	23 (15.3%)
Cough	1 (0.7%)	1 (0.1%)	0 (0%)
Cramping	1 (0.7%)	1 (0.1%)	0 (0%)
Dehydration	6 (4.0%)	8 (0.9%)	1 (0.7%)
Diarrhea	23 (15.3%)	29 (3.1%)	3 (2.0%)
Dizziness	40 (26.7%)	44 (4.7%)	4 (2.7%)
Epigastric Pain	2 (1.3%)	2 (0.2%)	0 (0%)
Eructation	77 (51.3%)	107 (11.4%)	25 (16.7%)
Esophageal Mucosal Tear	1 (0.7%)	1 (0.1%)	0 (0%)
Fever	1 (0.7%)	1 (0.1%)	0 (0%)
Gagging on Uvula	1 (0.7%)	1 (0.1%)	0 (0%)

Adverse Event[1]	# Subjects[2] with Events (% Subjects)	# Events[3] (% Events)	# Subjects with Event Occurrence > 1 (% Subjects)
Gas Pain	1 (0.7%)	1 (0.1%)	0 (0%)
Halitosis	32 (21.3%)	35 (3.7%)	3 (2.0%)
Headache	35 (23.3%)	43 (4.6%)	6 (4.0%)
Heartburn / Reflux	55 (36.7%)	75 (8.0%)	15 (10.0%)
Hiccups	33 (22.0%)	43 (4.6%)	6 (4.0%)
Intraoperative Bleeding	1 (0.7%)	1 (0.1%)	0 (0%)
Low Iron	1 (0.7%)	1 (0.1%)	0 (0%)
Malnutrition	1 (0.7%)	1 (0.1%)	0 (0%)
Metallic Taste in Mouth	1 (0.7%)	1 (0.1%)	0 (0%)
Nausea	105 (70.0%)	140 (15.0%)	22 (14.7%)
Night Sweats	1 (0.7%)	1 (0.1%)	0 (0%)
Pleural Effusion	1 (0.7%)	1 (0.1%)	0 (0%)
Pneumonitis	1 (0.7%)	1 (0.1%)	0 (0%)
Rash	1 (0.7%)	1 (0.1%)	0 (0%)
Rectal bleed	1 (0.7%)	1 (0.1%)	0 (0%)
Shortness of Breath	2 (1.3%)	2 (0.2%)	0 (0%)
Shoulder Pain	3 (2.0%)	3 (0.3%)	0 (0%)
Sore Throat	2 (1.3%)	2 (0.2%)	0 (0%)
Syncope	1 (0.7%)	1 (0.1%)	0 (0%)
Tremors	1 (0.7%)	1 (0.1%)	0 (0%)
Vomiting	74 (49.3%)	93 (9.9%)	10 (6.7%)
White Tongue	1 (0.7%)	1 (0.1%)	0 (0%)
Grand Total	138 (92.0%)	935 (100%)	132 (88.0%)

[1] Adverse Events reported in the CSR as a combination (i.e., Nausea and Vomiting) were separated into 2 events to ensure all related symptoms are reported together

[2] Subjects: N = 150

[3] Events: N = 935

Study Conclusions

The primary effectiveness analysis showed a higher responder rate in the Treatment group compared to Control group. A responder was defined as a patient who achieved at least 10%TBWL at 52 weeks after treatment or initiation of the lifestyle modification program. Weight loss was largely maintained over 104 weeks and the rate of device- and/or procedure-related SAEs was 7.3% (11/150; 95% CI: 3.7-12.7%). The observed rate of device or procedure related, Clavien-Dindo Grade III or higher, events was 2.3% (3/131) and the upper limit of the 95% confidence interval was 6.5%. Adverse events were mostly associated with symptoms of early accommodation to the sleeve (e.g. abdominal pain, eructation, nausea and vomiting) and resolved with medical intervention. The MERIT Trial demonstrated a favorable benefit:risk profile.

ESG Technique

Procedural Setup and Ancillary Equipment

Endoscopic sleeve gastroplasty (ESG) should be performed under general anesthesia with the patient positioned in a supine or semi supine left position to facilitate a safety margin between the stomach and surrounding structures.

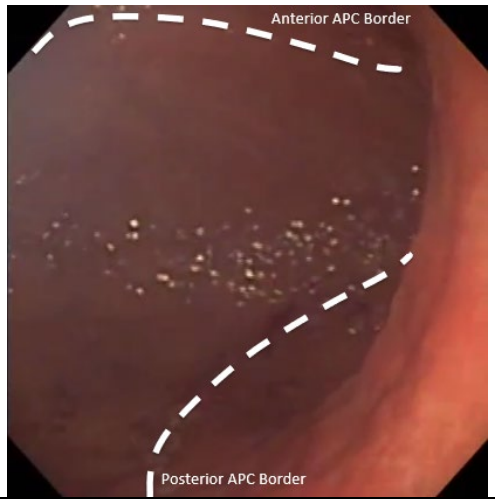
If using an overtube, verify compatibility between the overtube and the suturing device, as mounted on the specific endoscope. Lubricate the overtube and endoscope liberally. Place the overtube following the overtube manufacturer's directions.

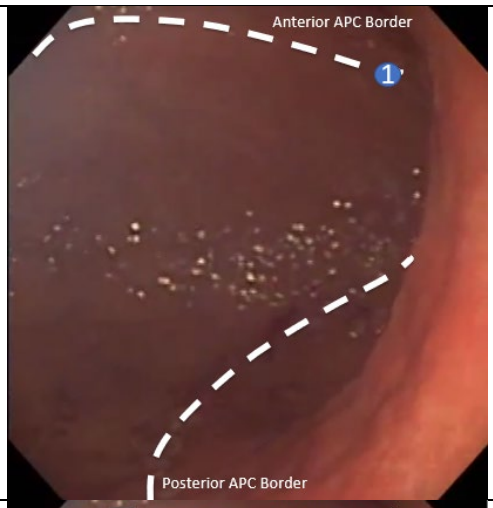
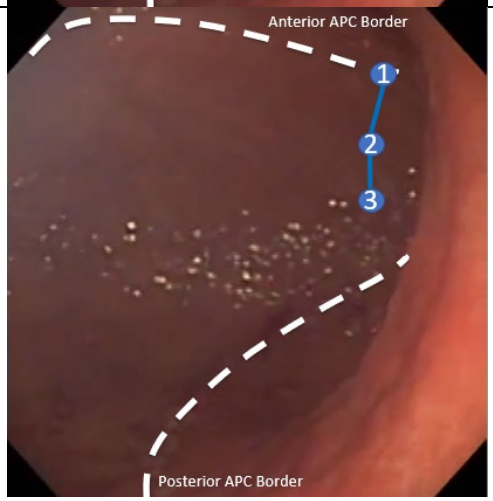
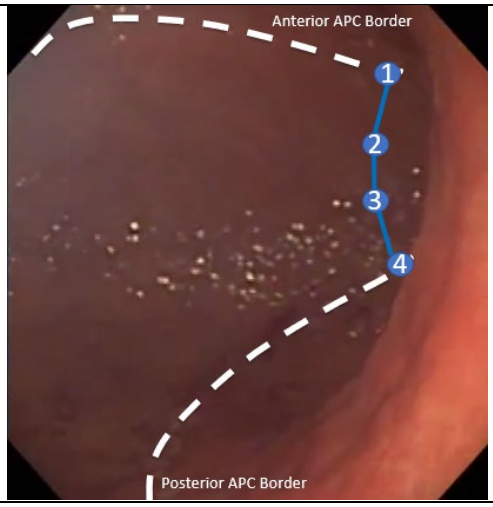
Coagulation marking on the mid-anterior and mid-posterior walls of the stomach is recommended to guide placement of stitches. Take care when using plasma coagulation marking. Perforation could occur while using plasma coagulation and/or coagulated tissue may slough off later, resulting in delayed gastrointestinal bleeding.

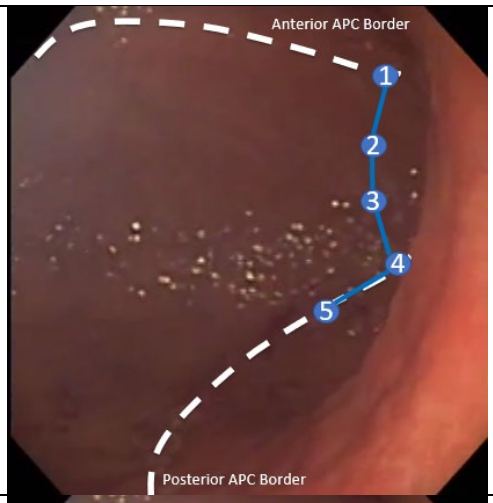
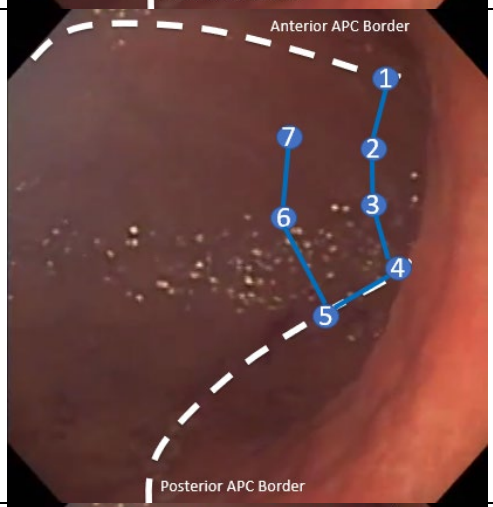
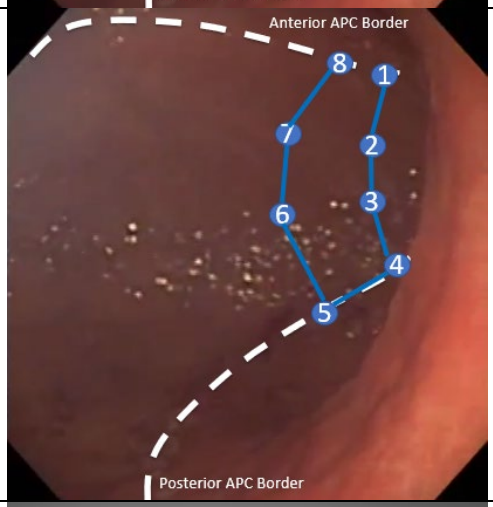
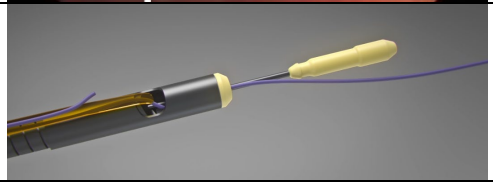
Carbon Dioxide (CO_2) is required for insufflation. Room air must not be used and can contribute to serious adverse events including pneumoperitoneum, pneumothorax, pneumomediastinum, and death.

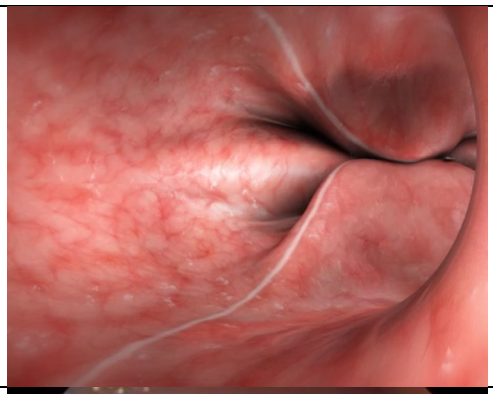
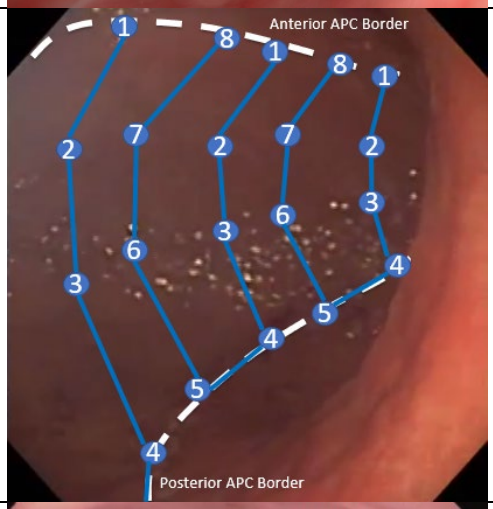
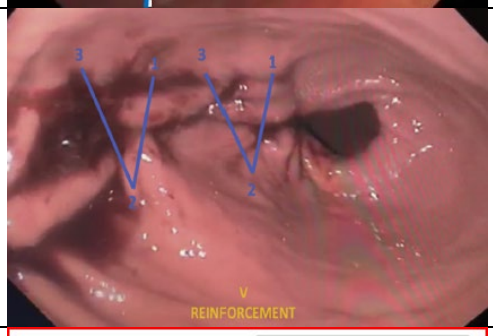
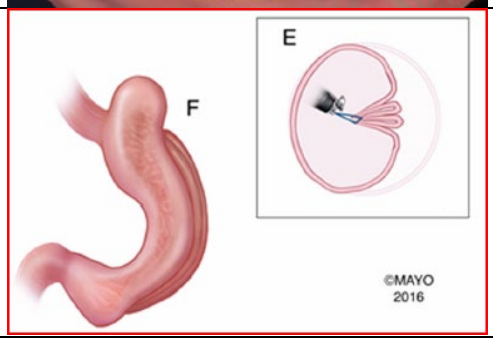
Endoscopic Sleeve Gastroplasty Procedure

Important factors for a successful procedure include properly operating the OverStitch device, successfully placing full thickness sutures at each position listed below, avoiding the fundus, and shortening the stomach length while decreasing the lumen diameter. Specific suture patterns are at the discretion of the physician but should begin in the distal stomach at the level of incisura and end proximally, before the fundus, the latter in order to reduce risk of an adverse event. Reinforcement sutures overlying the main plications are optional depending on the appearance of the stacked plications and sleeve lumen. The endoscopist should use the Helix to capture the muscle layer only (and not beyond), by avoiding excessive forward pressure and rotations of the Helix.

• Prior to suturing, it is recommended to use an endoscope and a coagulation device to mark the mid-anterior and mid-posterior borders of the stomach.	1 c 

• The first bite or stitch should start at the level of incisura. The first stitch should target the mid-anterior wall of the stomach with deliberate maneuvering of the endoscope tip and the gastric wall (captured by the Helix) to fill the suturing device tower to enable a full thickness bite. A gap of at least 1-1.5 cm between the exit point and return point of suture at a bite or stitch site provides a visual affirmation that a full thickness stitch has been placed.	
• The second and third suture positions should be placed along the greater curvature of the stomach.	
• The fourth position targets the mid-posterior wall of the stomach.	

• Move 1- 2cm proximal to the fourth stitch or bite along the mid-posterior wall to place the fifth stitch.	
• Stitch position six and seven and target the greater curvature of the stomach moving towards the anterior border.	
• Final stitch position returns to the anterior wall of the stomach in line with the first stitch.	
• The anchor is dropped from the anchor exchange in the lumen and the suture cinch is loaded with the proximal end of the suture.	

• The suture cinch is advanced into the scope and into the lumen to the first stitch site. The suture is tensioned against the cinch slowly to allow tissue approximation. Care should be taken not to over tension the suture and risk breakage. When appropriately snug tissue approximation is achieved, the cinch is deployed. The cinch catheter and excess suture is removed from the scope channel.	
• The suture pattern is repeated moving proximal approximately up to 2cm for each new plication, until the fundus is reached.	
• Final inspection of the lumen is performed, and full thickness reinforcement sutures may be placed with care not to interfere with the first row of sutures.	
• Illustration of the final sleeve.	

Prophylaxis Techniques to Consider

The endoscopist should use the Helix to capture the muscle layer only (and not beyond), by avoiding excessive forward pressure and rotations of the Helix.

To minimize the risk of early post-procedure dehydration, intravenous fluid hydration should be continued during the postoperative recovery period and based on the patient medical history.

To reduce the risk of infection, it is recommended to administer intravenous antibiotic prophylaxis before the procedure.

To reduce the risk of thromboembolic events, patients should receive prophylaxis with low-molecular weight heparin, if the procedure is expected to be prolonged. In selected cases, intermittent pneumatic compression devices should be placed on the lower extremities during the procedure.

To reduce the risk of post-procedure bleeding, avoid non-steroidal anti-inflammatory drugs before and after the procedure.

Patients on chronic antithrombotic therapy should be on a prescribed regimen established by the medical team managing these medications before, during and after the procedure.

ESG follow-up care

Most patients having ESG can be discharged the same day, though some may require a hospital stay to manage early symptoms of accommodation (e.g dehydration, pain, nausea or bleeding).

Following ESG, patients should be prescribed a clear liquid diet for several days with a gradual dietary progression and encouragement to maintain hydration, especially during the early post-procedure period.

Post-procedural abdominal pain and nausea are common and are expected to be self-limiting. These tend to resolve in the first week. These can be minimized with oral analgesics and anti-emetics. In some cases, more severe abdominal pain may require hospitalization with parenteral opioids. Rarely, post procedure discomfort with pain and nausea may be unrelenting and debilitating enough such that the plications should be endoscopically removed.

Upper GI bleeding has been reported post-procedure, as have hematemesis and melena. These typically present within the first week of the procedure but have been reported out to one month. In patients presenting with post-procedure bleeding and a drop in hematocrit or hemoglobin, perform endoscopy to inspect the sleeve. If bleeding is identified, it can be treated with conventional techniques or oversewing the bleeding site. Patients who develop significant persistent upper abdominal pain at any time after an ESG, with radiation to the back or supraclavicular area along with pleuritic symptoms or even dyspnea, may have developed a needle puncture site leak with the development of a sterile or infected fluid collection and inflammatory pleural effusion. These symptoms would warrant investigation with an imaging study, e.g. CT. Treatment includes the use of antibiotics, percutaneous drainage, or, if the leak can be identified, surgery.

Gastric perforation is a rare event and may be diagnosed by clinical presentation with peritonitis with free air and fluid in the abdominal cavity on imaging. These must be repaired either endoscopically or surgically.

Patients should progress to a full liquid diet, including 60 grams of protein per day, followed by progression to soft, then full low fat diet over several week intervals, e.g. 2 weeks, depending on accommodation to the sleeve. Patients are encouraged to drink sufficient non-alcoholic fluids per day to avoid dehydration, e.g. 48-64 oz. Overeating is likely to induce a sensation of bloating and should be avoided. Patients should be advised to maintain a healthy lifestyle, including both diet and exercise. Weight loss is typically reported to increase progressively over the first one to two years after the ESG procedure. Most of the weight loss will happen within the first six months. If a patient reports a loss of satiety or weight regain, they should be advised to consult with their doctor. The sleeve may need to be revised.

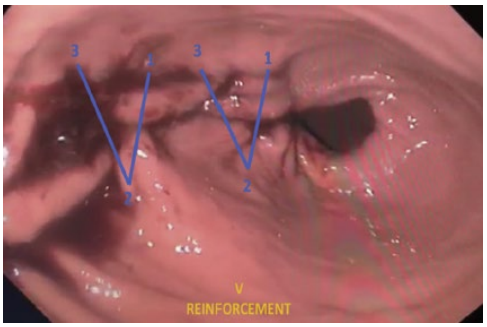
Addressing Weight Regain Following ESG, LSG or Gastric Bypass.

Some patients will lose weight after a bariatric procedure and then begin to regain weight. They may report that they can consume more food during a meal and no longer feel full after eating. Depending on the previous procedure, this can be an indication of plications coming apart, dilation of the sleeve or dilation of the gastric outlet and the gastric pouch. The following sections describe revision strategies for each of these situations. APOLLO REVISE may be used for these revisional procedures, as fewer suture-anchors are required.

ESG Retightening

These revision procedures require adherence to the same operating principles described for a primary ESG procedure. These general techniques include placement of full thickness bites, creation of lumen-narrowing, and multi-bite plications in a distal to proximal progression beginning at the incisura. Deep fundal plications must be avoided to reduce the risk for leak.

- Inspect the stomach to determine whether all or some plications have completely disappeared and if plications have loosened with exposed lengths of suture between stitch sites.
- Identify exposed needle anchors and cinches. These should be avoided or removed.
- In those cases where plications are absent, new plications are placed using the same suture pattern from the index procedure, with the first stitch or bite on the anterior wall.
- Extra care is taken to be certain that each stitch or bite is full thickness (1-1.5 cm gap between suture exit and entrance with each bite).
- It is recommended to place a second overlying reinforcing "V" set of 3 stitches (anterior, greater curve, posterior) in these cases.



- In cases where plications are intact but "loosened" with exposed lengths of suture, new plications are placed next to the loosened plications using the extra measures of second layer reinforcing suturing. The loosened plications are first released by cutting the exposed suture and removing suture to expose the area for the new plication.
- The new plications are created using the same technique as described above (*Endoscopic Sleeve Gastroplasty Procedure*).

Revision of LSG to Tighten the Sleeve

- The initial endoscopic inspection assesses whether the sleeve is dilated along the entire length or proximally, with an accompanying enlarged fundal remnant.
- Identify the staple line. Suturing through the staple line is to be avoided as it can damage the suture-anchor or suturing instrument.
- Coagulation marks can be made on the anterior and posterior walls. This can prevent closing the sleeve lumen beyond a desirable diameter (<1.5 cm).
- Fewer stitches are needed within the dilated sleeve to create plications. This is influenced by the starting lumen diameter and the staple line.
- Suturing is initiated on the anterior wall of the sleeve, incisura level.

- Extra care is taken to obtain full thickness bites. The tissue grasped by the Helix should be pulled into the device slowly to observe whether or not the grasped tissue is readily drawn into the device. If the grasped tissue is immobile, a deep tear can occur. In this setting, a different site should be selected for stitch placement.
- Plications are started distally.
- The dilated fundal remnant can be reduced with a plication. Care is taken to avoid the thinner cephalad or deeper portion of the remnant fundus to prevent leak.

Prophylactic Techniques and Follow-Up Care are consistent with the advice given in the section on ESG.

Conversion to Laparoscopic Sleeve Gastrectomy (LSG)

Patients receiving ESG may be converted to LSG if they begin to regain weight after achieving some or all of their weight loss goals. This can occur if the sleeve dilates, or the plications fail. An endoscopy is performed to identify and remove sutures, cinches and suture-anchors prior to performing the conversion. There is a risk of stapling over the original ESG hardware, which can damage the staples or jam the stapling instrument. Once the original ESG hardware is removed, the sleeve gastrectomy can be performed per the routine procedure.

Transoral Outlet Reduction (TORe)

Patients having previous Roux-en-Y gastric bypass bariatric surgery may experience dilation of the gastrojejunostomy outlet and the gastric pouch, followed by weight gain. This can be addressed by reducing the diameter of the gastric outlet by suturing. Often, the physician may elect to use additional suturing to reduce the dilated areas of the pouch. This procedure is often referred to as Transoral Outlet Reduction (TORe). These sutures can be applied using the APOLLO REVISE.

The TORe procedure is appropriate when a previous bypass patient demonstrates a stoma diameter greater than 20 mm (Abu Dayyeh 2011, Jaruvongvanich 2020) and is regaining weight. Jaruvongvanich (2020) conducted a meta-analysis and reported that the TORe procedure with full thickness suturing (n=737 patients), reduced the stoma diameter to 8-10mm and delivered an average of 8.1-11.0% TBWL through 6 months and 4.3-7.1 %TBWL at 12 months. This was consistent with the experience in a registry conducted by the American Gastroenterological Society through 12 months as well as Jirapinyo (2020), which reported weight loss of 8.8% TBWL at 5 years. The most common risks associated with the TORe procedure are bleeding (associated with the use of plasma coagulation) and stricture of the outlet, which can be addressed with endoscopic dilation using a balloon.

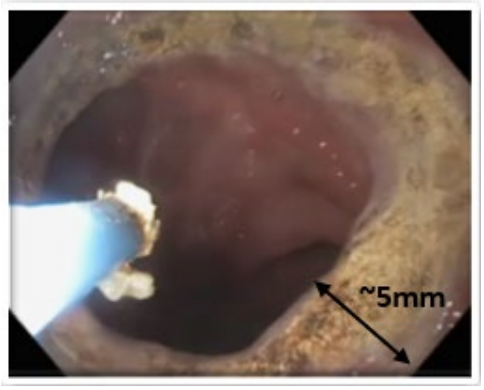
The sources of this information on TORe include the following.

- A multicenter registry on endoscopic suturing conducted as a partnership between Apollo Endosurgery and the American Gastroenterological Association. That study included 39 subjects having the TORe procedure.
- An ongoing single site registry made available to Apollo Endosurgery, including 201 subjects enrolled at a private bariatric practice.
- Abu Dayyeh BK, Lautz DB, Thompson CC. Gastrojejunal stoma diameter predicts weight regain after Roux-en-Y gastric bypass. Clinical Gastroenterology and Hepatology 2011; 9: 228-233.
- Jirapinyo P, Kumar N, AlSamman MA et al. Five-year outcomes of transoral outlet reduction for the treatment of weight regain after Roux-en-Y gastric bypass. Gastrointest Endosc 2020; May;91(5):1067-1073.
- Jaruvongvanich V, Vantanasiri K, Laoveeravat P et al. Endoscopic full thickness suturing plus argon plasma coagulation versus argon plasma mucosal coagulation alone for weight regain after gastric bypass: a systematic review and meta-analysis. Gastro Endo 2020; 92(6): 1164-1175.

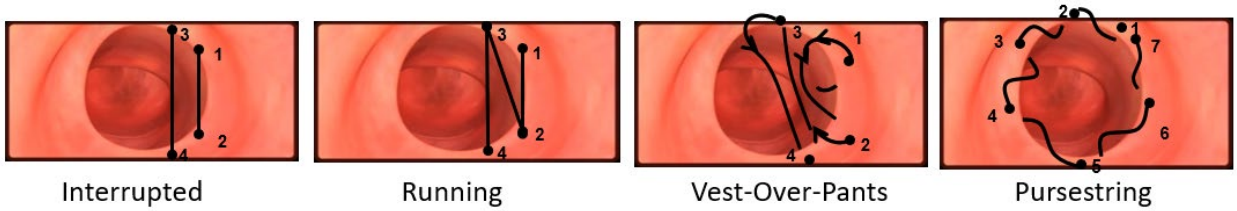
Important factors for a successful procedure include properly operating the device, successfully placing full thickness sutures at each position listed below, avoiding previously placed hardware, reducing the diameter of the gastric outlet

and then decreasing the pouch diameter (if applicable). Specific suture patterns are at the discretion of the physician but should begin with reducing the gastric outlet then reducing the gastric pouch, as necessary.

- Inspect the pouch to assess the size. A normal pouch is approximately 2 cm in length and no more than 2 cm in width.
- Inspect the gastrojejunal anastomosis. A normal anastomosis diameter should be < 1.5 cm.
- Reduce the dilated anastomosis first.
- Start by thoroughly coagulating the margin of the anastomosis and the pouch mucosa within 1 cm of the margin to destroy the mucosa. Alternatively, a circumferential endoscopic mucosal resection (EMR) can be performed to remove the mucosa to the edge of the anastomosis.



- Reduce the anastomosis at one side by placing full thickness stitches across from the jejunal to gastric side using the suture pattern of choice. The reduced lumen should be less than 1 cm.



- The anastomosis can be reduced by placing an 8- or 10-mm dilating balloon first, then tensioning the suture and cinching around the balloon.
- If the pouch is dilated, plications can be created to close the lumen to a diameter of less than 2 cm. Fewer stitches are needed compared to a primary ESG plication and are determined by the beginning size of the pouch.
- Stitch placement is guided by the shape of the pouch.
- More than one plication may be needed for the pouch reduction. A plication can be placed to a level just below the squamocolumnar junction.
- When creating a plication below the squamocolumnar junction, placing stitches within the lesser curve should be avoided to reduce the risk for bleeding.
- Prophylactic Techniques and Follow-Up Care are consistent with the advice given in the section on ESG.

Disposal

Dispose of any used of explanted devices or components in accordance with local regulations for medical waste.

MRI Safety Information

MR Conditional 

Non-clinical testing has demonstrated that the Suture-Anchors and Cinch included in the APOLLO ESG SX and APOLLO REVISE SX are MR Conditional. A patient implanted with these components can be safely scanned immediately after placement in an MR system meeting the following conditions:

Static Magnetic Field

- Static magnetic field of 1.5 T or 3.0 T.
- Maximum spatial field gradient of 2,000 gauss/cm (20 T/m).
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2 W/kg.

Under the scan conditions defined above, the implanted device construct is expected to produce a maximum temperature rise of less than 2º C after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the implanted device construct extends approximately 10 mm from this device when imaged with a gradient echo pulse sequence and a 3.0 T MRI system.

Table 13: Symbols Used on Product Labeling

Symbol	Description	Symbol	Description
	Caution. See Instructions for Use		Sterilized Using Ethylene Oxide
	Consult Instructions for Use.		MR Conditional
	Manufacturer		Use By Year, Month, & Day
	Reference Number		Single Use Only. Do Not Re-use.
	Serial Number		Do not use if package is damaged
	Lot Number		Prescription Use Only

APOLLO ENDOSURGERY, INC.
1120 South Capital of Texas Highway
Building 1, Suite 300
Austin, TX 78746 USA
855-551-3123

www.apolloendo.com

GRF-00548-00R01
2022-07