Solesta® Package Insert

CAUTION: Federal Law restricts this device to sale by or on the order of a physician.

Indication for Use

Solesta® is indicated for the treatment of fecal incontinence in patients 18 years and older who have failed conservative therapy (e.g., diet, fiber therapy, anti-motility medications).

Device Description

Solesta consists of dextranomer microspheres, 50 mg/mL, and stabilized sodium hyaluronate, 15 mg/mL, in phosphate-buffered 0.9% sodium chloride solution.

Solesta is a sterile, viscous, biocompatible bulking agent contained in a disposable 1 mL assembled glass syringe with a standard Luer-lock fitting. The syringe is equipped with a plunger stopper, a plunger rod and a finger grip. The labeled syringe is packed in a pouch and terminally sterilized by moist heat. The final product consists of a carton containing four pouches with syringes, five sterile needles (Sterican®, 21G x 4 ¾ inches, 0.80 x 120 mm), patient record labels and a package insert. The product is for single use.

Both the dextranomer and sodium hyaluronate are made up of biosynthesized polysaccharides of non-animal origin. The dextranomer component consists of microspheres of dextran chains cross-linked into a three-dimensional network. The stabilized sodium hyaluronate accounts for the viscous properties of Solesta and acts as a carrier that facilitates the injection of the dextranomer microspheres.

Solesta is injected in the deep submucosal layer in the proximal part of the high pressure zone of the anal canal about 5 mm above the dentate line. A total of four submucosal injections of 1 mL Solesta are administered at each treatment session.

Contraindications

Solesta is contraindicated in patients with the following conditions:

- Active inflammatory bowel disease
- Immunodeficiency disorders or ongoing immunosuppressive therapy
- Previous radiation treatment to the pelvic area
- Significant mucosal or full thickness rectal prolapse
- Active anorectal conditions including: abscess, fissures, sepsis, bleeding, proctitis, or other infections
- Anorectal atresia, tumors, stenosis or malformation
- Rectocele
- Rectal varices
- Presence of existing implant (other than Solesta) in anorectal region
- Allergy to hyaluronic acid based products

Warnings

- Do not inject Solesta intravascularly. Injection of Solesta into blood vessels may cause vascular occlusion.
- Injection in the midline of the anterior wall of the rectum should be avoided in men with enlarged prostate.

Precautions

General precautions

- Solesta should only be administered by physicians experienced in performing anorectal procedures and who have successfully completed a comprehensive training and certification program in the Solesta injection procedure.
- The safety and effectiveness of Solesta have not been investigated in patients with complete external sphincter disruption or significant chronic anorectal pain.
- The safety and effectiveness of Solesta have not been investigated in patients with previous procedures involving the anorectal region: rectal anastomosis <12 cm from anal verge, anorectal surgery within previous 12 months, hemorrhoid treatment with rubber band within 3 months, anorectal implants and previous injection therapy, Stapled Transanal Rectal Resection (STARR) or stapled hemorrhoidectomy.
- The safety and effectiveness of Solesta have not been studied in patients under the age of 18 years.
- The safety and effectiveness of Solesta have not been studied in pregnant or breastfeeding women.
- The durability of Solesta has not been studied past 12 months.
- The safety and effectiveness of Solesta have been studied in patients who received one or two treatments. In the Pivotal study, the majority of patients received two treatments, four weeks apart.

Patient related precautions

- Patients with bleeding diathesis or patients using anticoagulant or antiplatelet agents, as with any injections, may experience increased bleeding at injection sites.
- Patients should be counseled that a repeated Solesta injection procedure may be required to achieve a satisfactory level of improvement in incontinence.

Procedure related precautions

- Adequate bowel preparation of the rectum using enema is required prior to injection. The enema should be given immediately prior to the procedure to ensure evacuation of the anorectum. It is recommended that additional cleansing of the injection area with an antiseptic be performed prior to injection. Use of prophylactic antibiotics is recommended.
- Solesta should be injected slowly to avoid undue stress on the Luer-lock connection which could cause leakage of the gel.
- After injection of Solesta, hold the needle at the injection site for an additional 15-30 seconds to minimize leakage of Solesta.
- Injections too close to the dentate line or too deep in the tissue might cause excessive pain.
- Injection should be stopped if excessive bleeding or pain occurs.
- One sterile needle should be used per syringe and injection.

Device related precautions

- The use of needles other than those supplied may impede injection of Solesta due to the properties of the gel and may cause device malfunction.
- Solesta is supplied ready to use in a prefilled syringe with a Luer-lock fitting. Carefully examine the unit to verify that neither the contents nor the package has been damaged in shipment. Do not use if damaged.
- Solesta is supplied sterile and is intended for single use only. Do not re-sterilize, as this may damage or alter the product.
- In the event of accidental contamination of a needle, discard the needle.
- Never mix Solesta with other products.
- Solesta is to be stored at up to 25°C (77°F), and used prior to the expiration date printed on the label. Do not expose Solesta to either sunlight or freezing, as this may damage or alter the product.
- Care should be taken when handling the glass syringes and disposing of broken glass to avoid laceration or other injury.
- After use, syringes and needles should be handled as potential biohazards. Disposal should be in accordance with accepted medical practice and applicable local, state and federal requirements.

Adverse Events

Potential adverse events include: abdominal discomfort, abdominal distension, abdominal pain, lower abdominal pain, abdominal rigidity, alopecia, anal abscess, anal fissure, anal hemorrhage, anal prolapse, anal pruritus, anorectal discomfort, back pain, constipation, C-reactive protein increased, chills, cold sweat, defecation urgency, dermatitis, diarrhea, device dislocation, dizziness, dyspareunia, escherichia bacteremia, fecal incontinence, feces hard, fatigue, gastrointestinal motility disorder, gastrointestinal pain, genital discharge, genital prolapse, hematochezia, hematospermia, hemorrhoids, infection, injection site abscess, injection site discomfort, injection site hemorrhage, injection site hematoma, injection site inflammation, injection site irritation, injection site nodule, injection site pain, injection site pustule, injection site swelling, injection site ulcer, intestinal mass, malaise, mucosal inflammation, musculoskeletal pain, perineal abscess, nausea, edema, pain, painful defecation, pelvic mass, perineal pain, proctalgia, proctitis, pyrexia, rectal abscess, rectal discharge, rectal hemorrhage, rectal lesion, rectal obstruction, rectal prolapse, rectal spasm, rectal tenesmus, rectovaginal septum abscess, urinary retention, vaginal discharge, vulvovaginal pain. The adverse event profile of Solesta beyond 18 months is not known, but is under investigation in post-market studies.

The observed adverse events are discussed in the Clinical Studies section below.

Clinical Studies

Introduction

Clinical data supporting the safety and effectiveness of Solesta are available from three clinical studies: 1) a pivotal, prospective, multicenter, randomized, sham-controlled double-blind study of 206 patients conducted under an Investigational Device Exemption (IDE; Pivotal study), 2) a prospective, multicenter, open-label study of 115 patients conducted outside the United States (Open-Label study), and 3) a single center study of 34 patients conducted at one site in Sweden (Proof-of-Concept study). The Pivotal study also included a cross-over option for patients initially randomized to Sham. The majority of patients (over 84%) in all three studies were female.

Table 1 provides an overview of the design of the three studies.

Table 1. Comparison of the three clinical studies supporting safety and effectiveness of Solesta

	Pivotal study	Open-Label study	Proof-of-Concept study
Study Design	Randomized double-blind comparative study of Solesta versus Sham in 2:1 ratio	Open study	Open study
Primary Efficacy Endpoints	Effectiveness: (1) Superiority in proportion Responder$_{50}$ compared with Sham at 6 months (2) Durability of response based on proportion responders at 12 months	Effectiveness: Proportion Responder$_{50}$ at 12 months	Effectiveness: Proportion Responder$_{50}$ at 12 and 24 months
Secondary Efficacy Variables	Fecal Incontinence Quality of Life (FIQL) Scale	FIQL	SF-36 European Organization for Research and Treatment of Cancer (EORTC) QLQ-C30
	Cleveland Clinic Florida Incontinence Score (CCFIS)	CCFIS	Miller Score
	Fecal Incontinence (FI) free days	FI free days	FI free days
	Fecal Incontinence (FI) episodes, controlled bowel emptying, medications	FI episodes, controlled bowel emptying, medications	FI episodes, global evaluation by patient, patient subjective judgment of treatment effect
Investigational Centers	8 centers in US and 5 centers in Europe	14 centers in Europe and 1 center in Canada	1 center in Sweden
Sample Size	136 patients randomized to Solesta, and 70 patients randomized to Sham	115 patients	34 patients
Inclusion Criteria	Age 18-75 years	Age 18-80 years	Age 18-80 years
	≥4 FI episodes over 14 days in patient diary	≥4 FI episodes over 28 days in patient diary	At least one FI episode weekly
	CCFIS≥10	CCFIS≥5	Miller score ≥6
	Solid or liquid FI episodes	Solid or liquid FI episodes	Solid or liquid FI episodes
	Failed conservative treatment	Failed conservative treatment	
Exclusion Criteria	Complete external sphincter disruption, significant mucosal prolapse	Complete external sphincter disruption, significant mucosal prolapse	Complete external sphincter disruption, significant mucosal prolapse
Retreatment Criteria	Incontinent at one month after initial treatment and CCFIS ≥10	Incontinent at one month after initial treatment	Some subjective improvement but less than 50 % reduction in FI episodes

The Pivotal study is the primary data set that demonstrates the safety and effectiveness of Solesta. The Open-Label and Proof-of-Concept studies provide supporting evidence of safety and effectiveness.

Treatment Information

Pre-operative Bowel Preparation

Pre-treatment evacuation of the rectum was done with an enema in the majority of the patients in all 3 studies. A small number of patients received topical antiseptic cleansing at the discretion of the treating physician. Prophylactic antibiotics were administered to individual patients in the Pivotal study at the discretion of the treating investigator and only 15 patients at 3 sites received prophylactic antibiotics in this study. No patients in the Open-Label study received prophylactic antibiotics.

Treatment Procedure

The Solesta injection procedure was the same in all 3 studies. Treatment was administered in an out-patient setting without anesthesia. Four equally spaced injections were administered through an anoscope and placed about 5 mm proximal to the dentate line. Treatment volume was generally 4 x 1 mL per treatment session. A single re-treatment procedure was offered to patients with persistent fecal incontinence after approximately 1 month. The maximum total treatment dose was 8 mL. In the Pivotal study, the sham injection procedure consisted of using 4 separate syringes to pierce the mucosa. The syringes were held in place for the same amount of time as Solesta injection: however, nothing was injected.

Patient Demographics

Both of the multicenter studies enrolled subjects with a broad range of age and body mass index. The majority of patients enrolled in both studies were females. Over 10% of patients enrolled in the Pivotal study were African-Americans, Hispanics or Asians. The causes of FI in both studies were attributed mainly to obstetric cause, neurogenic cause, and iatrogenic cause based on available medical history.

Table 2 provides an overview of the patient demographics in the Pivotal study. The Open-Label study and the Proof-of-Concept study enrolled patients with similar demographics.

Table 2. Demographics in the Pivotal study

Subject Demographics		Pivotal study (n=206)
Female	n (%)	183 (88.8)
Age, years	Mean (range)	60.1 (29.4–76.0)
Body Mass Index (BMI), kg/m^2	Mean (range)	27.1 (17.2–44.8)
Caucasian origin	n (%)	181 (87.9)
Duration of symptoms over 5 years	n (%)	106 (51.7)
Obstetric cause	n (%)	82 (39.8)
Neurogenic cause	n (%)	43 (20.9)
Iatrogenic cause	n (%)	46 (22.3)
Other cause (mostly idiopathic)	n (%)	35 (17.0)

Safety Data

The safety evaluation of Solesta in the treatment of fecal incontinence (FI) is based on the results from the Pivotal clinical study, and is supported by the Open-Label multicenter clinical study and one single site Proof-of-Concept study. The analysis of safety was based on the safety cohort of all 206 patients treated in the Pivotal study with either Solesta or Sham. Safety data for Solesta are available from 359 treatments in 197 total patients followed for up to 18 months post treatment (i.e., 136 subjects from the blinded phase and 61 subjects from the open phase).

The primary safety data set includes data from 206 patients treated with either Solesta or Sham in the Pivotal study. The data show that a total of 232 treatment-related adverse events for either Solesta or Sham were reported up to 18 months after treatment. Three (3) adverse events assessed as related to Solesta, or 1.3% of the treatment-related adverse events, were deemed serious by the investigators. These three (3) serious adverse events occurred in three (3) patients, including one case of an E. coli bacteremia, and two (2) cases of rectal abscesses (one event per patient). All of these serious adverse events resolved following treatment without any sequelae within approximately 30 days of treatment. Overall, 96% of the 203 Solesta treatment-related adverse events in the Pivotal study were of mild to moderate intensity and 97% of the events required no intervention or required medical or simple non-invasive interventions, including application of local pressure, silicone ointment, water irrigation and warm baths. Seven (7) events required more invasive procedures including: perianal drainage of abscesses (4 events), one (1) case of rubber band ligation of an anal prolapse, one (1) case of lancing of a hemorrhoid, and one (1) case of a Kenalog injection in a pre-existing anal scar. As shown in Table 3, the most frequent adverse events following Solesta treatment pertained to post-treatment proctalgia, minor anal or rectal bleeding, post-treatment fever, abdominal complaints (such as diarrhea and constipation), and events potentially related to peri-operative infection.

Combined with the supportive studies, a total of 346 patients received 566 treatments with Solesta. All three studies utilized similar inclusion/exclusion criteria and all three studies used exactly the same procedure for administering Solesta. The multi-center Open-Label study demonstrated similar safety results as the Pivotal study. A total of 163 AEs were reported by 71 of the 115 patients treated with Solesta in the study. Of these AEs, 79 AEs reported by 44 patients (38%) were assessed by the investigators to be related to the study treatment. Thus, the incidence of treatment-related AEs per total number of performed treatments was 51.3% (79 events/154 treatments). Similar to the Pivotal study, the five (5) most frequently reported types of treatment-related AEs were proctalgia, pyrexia, constipation, diarrhea and injection site pain. Six (6) treatment-related AEs reported in 4 patients were classified as serious in the study. Three (3) of these serious and treatment-related adverse events were cases of abscess reported by three (3) patients and the remaining three (3) were reported by a single patient who had a rectal prolapse with concurrent rectal bleeding and pain. In this latter case, tissues surrounding a Solesta bulge had prolapsed downwards in the anal canal and the Solesta bulge was excised in surgery.

In the Proof-of-Concept study, 34 patients were treated in the study and 33 patients were followed for 24 months. In total, 53 treatments with Solesta were administered in the study. These patients experienced a total of 86 treatment-related adverse events that were reported by 29 patients. No treatment-related adverse event was reported as serious. The duration was 1- 4 days for most events and all events were resolved within 1 week. No adverse events occurred after month 12. One (1) patient gave birth to a healthy child approximately 18 months after treatment and the delivery was a normal vaginal delivery. The observed adverse events were similar to those seen in the Pivotal study.

Table 3. Related adverse events (including serious AEs) for patients with blinded or open-label treatment with Solesta through month 18 in the Pivotal study. MedDRA Preferred Term. Safety population, (n=197)

MedDRA Preferred term	Number and (%) of patients	Number of events	Maximum intensity			Median (days)		Intervention			% of events resolved
			Mild	Moderate	Severe	Time to onset	Duration	None	Medical treatment	Other*	
Abdominal discomfort	1 (0.5)	1	.	1	.	1.0	6.0	.	.	1	100%
Abdominal distension	1 (0.5)	1	.	1	.	0.0	3.0	1	.	.	100%
Abdominal pain	1 (0.5)	1	.	1	.	68.0	52.0	.	1	.	100%
Abdominal pain lower	2 (1.0)	2	2	.	.	30.5	60.0	2	.	.	100%
Abdominal rigidity	1 (0.5)	1	.	1	.	196.0	.	.	1	.	0% †
Alopecia	1 (0.5)	1	.	.	1	6.0	189.0	1	.	.	100%
Anal abscess	1 (0.5)	1	.	1	.	139.0	44.0	.	.	1	100%
Anal fissure	2 (1.0)	2	1	1	.	90.5	228.0	.	2	.	100%
Anal hemorrhage‡	8 (4.1)	9	7	2	.	1.0	4.0	7	.	2	100%
Anal prolapse	3 (1.5)	3	2	1	.	287.0	2.0	1	.	2	100%
Anal pruritus	3 (1.5)	4	4	.	.	49.0	72.0	3	1	.	100%
Anorectal discomfort	8 (4.1)	8	7	1	.	2.0	21.0	3	5	.	100%
Back pain	1 (0.5)	1	1	.	.	70.0	113.0	.	.	1	100%
C-reactive protein increased	1 (0.5)	1	.	1	.	11.0	18.0	.	1	.	100%
Chills	4 (2.0)	4	1	2	1	0.5	4.5	4	.	.	100%
Cold sweat	1 (0.5)	1	.	1	.	0.0	3.0	1	.	.	100%
Constipation	3 (1.5)	3	3	.	.	3.0	2.0	1	2	.	100%
Defecation urgency	2 (1.0)	2	2	.	.	2.5	4.5	1	1	.	100%
Dermatitis	1 (0.5)	1	1	.	.	90.0	79.0	.	.	1	100%
Device dislocation	1 (0.5)	1	1	.	.	260.0	14.0	.	.	1	100%
Diarrhea	8 (4.1)	10	9	1	.	2.5	5.0	4	6	.	100%
Dyspareunia	2 (1.0)	2	2	.	.	65.0	60.5	2	.	.	100%
Escherichia bacteremia	1 (0.5)	1	.	1	.	0.0	36.0	.	1	.	100%
Fecal incontinence	1 (0.5)	1	.	1	.	0.0	64.0	1	.	.	100%
Feces hard	1 (0.5)	1	1	.	.	15.0	63.0	1	.	.	100%
Fatigue	1 (0.5)	1	.	1	.	0.0	3.0	1	.	.	100%
Gastrointestinal motility disorder	1 (0.5)	1	1	.	.	226.0	117.0	1	.	.	100%
Gastrointestinal pain	1 (0.5)	1	.	1	.	0.0	8.0	1	.	.	100%
Genital prolapse	1 (0.5)	1	.	1	.	1.0	10.0	.	.	1	100%
Hemorrhoids	1 (0.5)	1	.	1	.	0.0	6.0	.	.	1	100%
Injection site hemorrhage‡	16 (8.1)	18	18	.	.	0.0	1.0	17	.	1	100%
Injection site inflammation	1 (0.5)	1	1	.	.	0.0	5.0	.	1	.	100%
Injection site irritation	1 (0.5)	1	1	.	.	28.0	8.0	1	.	.	100%
Injection site nodule	1 (0.5)	1	1	.	.	294.0	99.0	1	.	.	100%
Injection site pain	10 (5.1)	10	7	3	.	0.0	1.5	9	1	.	100%
Injection site pustule	1 (0.5)	1	1	.	.	0.0	22.0	.	1	.	100%
Injection site swelling	1 (0.5)	1	1	.	.	0.0	78.0	1	.	.	100%
Intestinal mass	1 (0.5)	1	1	.	.	196.0	14.0	.	.	1	100%
Mucosal inflammation	1 (0.5)	1	1	.	.	27.0	74.0	1	.	.	100%
Musculoskeletal pain	1 (0.5)	1	1	.	.	358.0	183.0	1	.	.	100%
Nausea	1 (0.5)	1	1	.	.	0.0	3.0	1	.	.	100%
Pain ("body aches")	2 (1.0)	2	.	1	1	1.5	5.0	2	.	.	100%
Painful defecation	2 (1.0)	2	2	.	.	1.5	132.5	1	.	1	100%
Pelvic mass	1 (0.5)	1	.	1	.	2.0	27.0	.	1	.	100%
Perineal pain	1 (0.5)	1	.	1	.	0.0	5.0	1	.	.	100%
Proctalgia	34 (17.3)	41	20	21	.	1.0	8.0	14	19	8	97.6% §
Proctitis	5 (2.5)	5	2	2	1	5.0	16.0	2	3	.	100%
Pyrexia	13 (6.6)	14	12	1	1	1.0	6.0	5	8	1	100%
Rectal abscess	3 (1.5)	3	.	1	2	2.0	6.0	.	1	2	100%
Rectal discharge	7 (3.5)	7	6	1	.	2.0	4.0	4	2	1	100%
Rectal hemorrhage‡	15 (7.6)	15	11	4	.	7.0	3.0	13	1	1	100%
Rectal lesion	1 (0.5)	1	.	1	.	5.0	179.0	.	.	1	100%
Rectal obstruction	2 (1.0)	2	2	.	.	75.5	66.0	2	.	.	100%
Rectal spasm	1 (0.5)	1	.	1	.	133.0	50.0	1	.	.	100%
Urinary retention	1 (0.5)	1	1	.	.	8.0	20.0	1	.	.	100%
Vaginal discharge	1 (0.5)	1	1	.	.	0.0	5.0	1	.	.	100%
Vulvovaginal pain	1 (0.5)	1	.	1	.	0.0	6.0	.	1	.	100%
Totals	**103 (52.3)**	**203**	**136**	**60**	**7**	**1.0**	**6.0**	**115**	**60**	**28**	**99.0%**

* Other intervention included: follow up ultrasound, I & D of rectal abscess, Kenalog injection to anal area scar, rubber band ligation, observation, extra check-up at clinic, silicone or xylocaine ointment, examinations, blood tests, feces-Hb screen, outpatient visit to gynecologist, irrigation with water, lanced hemorrhoid, pressure, irrigation-dissection of abscess, flexible sigmoidoscopy, pelvic v/s scan, warm baths, drainage of anal abscess

† Outcome for one event pending at time of this summary report (patient withdrawn and event currently recorded as not recovered)

‡ AEs reported as bleeding were coded as "hemorrhage" at the preferred term level in MedDRA regardless of intensity

§ Outcome for one event pending at time of this summary report

Effectiveness

Primary Efficacy Objective - Pivotal Study

The Pivotal study included a primary efficacy objective composed of three parts. All three parts of the primary objective were met. The study was only powered for the primary endpoint and was not designed or powered to demonstrate a statistical difference between Solesta and Sham for the secondary efficacy endpoints.

Superiority was shown for Solesta (53.2%) versus Sham (30.7%) at 6 months (p=0.004; logistic regression), as illustrated in Figure 1, based on analysis of proportion Responder$_{50}$. Responder$_{50}$, defined as proportion of patients with a ≥50% reduction in number of incontinence episodes compared to baseline, has been used to objectively evaluate response to treatments for FI in other studies.

The second success criterion required that the results achieve a pre-specified minimum level of responders in the treatment group as defined by a lower confidence limit (LCL) of at least 35%. The LCL of the 95% confidence interval of the proportion Responder$_{50}$ at 6 months was 40.2%, as illustrated in Figure 2.

The third success criterion concerned durability of the treatment effect and required a minimum level of proportion Responder$_{25}$ (≥25% improvement from baseline) for Solesta at 12 months, as defined by a lower confidence limit of 50%. The LCL for proportion Responder$_{25}$ at 12 months was 61.4%, as illustrated in Figure 2.

As an additional supporting analysis, the proportion Responder$_{50}$ at 12 months after last treatment was also calculated and it was 57.4%, similar to the results at 6 months. Analyses were performed to determine whether there was any association between baseline or demographic characteristics and treatment response. No such relationship was found.

Figure 1. Comparison of proportion Responder$_{50}$ at 6 months

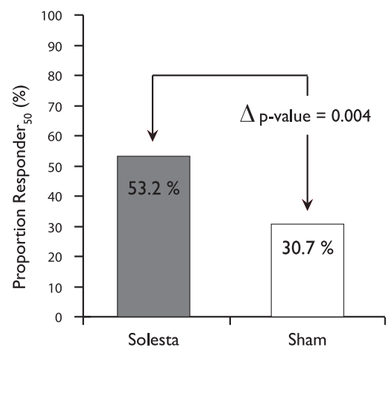
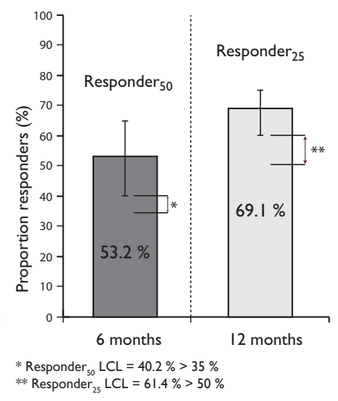


Figure 2. Solesta proportion responders at 6 and 12 months



* Responder$_{50}$ LCL = 40.2 % > 35 %

** Responder$_{25}$ LCL = 61.4 % > 50 %

Primary Endpoint Pivotal and Supporting Studies

All three studies show durability of the treatment effect to 12 months as evidenced by the proportion Responder$_{50}$. As shown in Table 4 the proportion Responder$_{50}$ at 6 months and 12 months were similar across all three studies.

Table 4. Summary of proportion Responder$_{50}$ at 6 and 12 months and at 24 months with Solesta treatment.

Proportion Responder$_{50}$ [95% CI]	Pivotal study (ITT, PIM)	Open-Label Study (ITT, OC)	Proof-of-Concept Study (OC)
6 months	53.2% [40.2–65.8] n= 136	57.1% [47.3–66.9] n=98	44.1% [27.4–60.8] n=34
12 months	57.4% [49.0–65.7] n=136	64.0% [53.8–74.1] n=86	55.9% [39.2–72.6] n=34
24 months	N/A	N/A	59.4% [42.4–76.4] n=32

CI = confidence interval; ITT = intent-to-treat; PIM = primary imputation model; OC = observed cases;
n = number of subjects

Secondary Endpoints for Pivotal and Supporting Studies

The following secondary endpoints were evaluated in the three clinical studies:

- Fecal incontinence episodes
- Fecal incontinence-free days
- Fecal Incontinence Quality of Life (FIQL) assessment
- Cleveland Clinic Florida Incontinence Score (CCFIS) or Miller Score

Fecal Incontinence Episodes

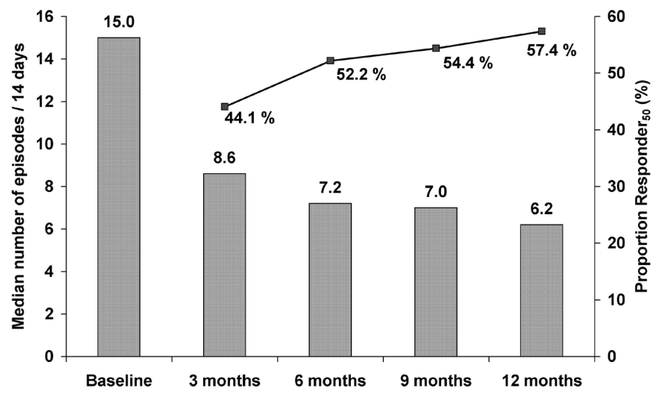
In the Pivotal study, reductions in number of FI episodes from baseline at both 3 and 6 months were observed in both the Solesta and Sham treatment groups. For the Solesta group the median FI episodes were shown to decrease from 15 episodes at baseline to 7.2 episodes at 6 months and 6.2 episodes at 12 months. For the Sham group the median FI episodes were shown to decrease from 12.5 episodes at baseline to 10.0 episodes at 6 months (see Table 5). Both the Solesta and Sham groups showed a change from baseline at 6 months, and the change from baseline in the Solesta group was larger than that observed for the Sham group. Similar reductions from baseline with Solesta treatment were observed in the Open-Label study and the Proof-of-Concept study.

Figure 3 shows the sustained improvement in Responder$_{50}$ analysis and reduction in fecal incontinence episodes over 12 months in the Pivotal study for the Solesta group only.

Table 5. Median number of fecal incontinence episodes/14 days for each treatment group and change from baseline 6 months. As observed. Last Observation Carried Forward (LOCF). ITT population (n=206 patients: Pivotal study)

Number of episodes	Solesta (n=136)	Sham (n=70)	Difference in median changes between groups (Solesta-Sham)
	Median	Median	
Baseline	15.0	12.5	
6 months	7.2	10.0	
Δ from baseline	-6.0	-3.0	-3.0
% Δ from baseline	-50.6	-22.6	-28.0

Figure 3. Median number of FI episodes and proportion Responder$_{50}$ at each follow up time point in the Pivotal study. Solesta ITT population (n=136)



Fecal Incontinence-free days

In all three studies, an increase in number of fecal incontinence-free days was observed with Solesta treatment. In the Pivotal study at 6 months, both the Solesta and Sham treatment groups experienced an increase in number of incontinence free days from their pre-treatment baseline values of 4.4 days and 4.8 days, respectively. However, the Solesta group demonstrated an increase of 3.1 fecal incontinence-free days when compared to the Sham group increase of 2.0 days. At 12 months, the increase in number of fecal incontinence-free days in the Solesta group was maintained at 3.4 days. Similar increases in number of fecal incontinence-free days with Solesta treatment were shown in the Open-Label study and the Proof-of-Concept study.

Fecal Incontinence Quality of Life assessment (FIQL)

The FIQL scale is a validated tool that is specifically designed to assess the impact of FI on a patient's quality of life. In the blinded phase of the Pivotal study, improvement in FIQL scores compared to baseline was observed in both the Solesta and Sham groups at 6 months. The change from baseline score was greater in the Solesta group than the Sham group in all four domains: Lifestyle (Δ=0.22), Coping/Behavior (Δ=0.25), Depression/Self perception (Δ=0.09) and Embarrassment domains (Δ=0.16), (see Table 6). In the Open-Label study, FIQL scores showed a similar improvement. The Proof-of-Concept study did not evaluate FIQL.

Cleveland Clinic Florida Incontinence Score (CCFIS)

The CCFIS is a validated measure of the impact of FI on patients. In the pivotal study, in both the Solesta and Sham groups, the CCFIS was improved as compared to baseline at 6 months. The difference at 6 months in mean change from baseline between the Solesta group and the Sham group was small (see Table 6). Solesta showed improvements from baseline at 12 months in both the Pivotal study and the Open-Label study.

The Proof-of-Concept study did not incorporate CCFIS but instead used the Miller Score, another assessment tool for FI. The Miller Score is based on a subject interview using standardized questions regarding incidence and type of incontinence (solid, liquid or gas). Improvements from baseline and sustained improvements were shown at 6, 12, and 24 months.

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Table 6. Secondary efficacy evaluations of difference in change from baseline between Solesta and Sham at 6 months. LOCF. ITT population (n=206 patients: Pivotal study)

Secondary endpoints	Score/Scale range	Estimate of mean change from baseline		Estimate of difference (95% CI)
		Solesta	Sham	
Fecal Incontinence Quality of Life (FIQL) scale (higher score = increased QoL)				
Lifestyle*	1-4	0.33	0.11	0.22 (0.04:0.40)
Coping/Behavior*	1-4	0.44	0.19	0.25 (0.08:0.43)
Depression/Self perception*	1-6	0.27	0.18	0.09 (-0.08:0.26)
Embarrassment*	1-4	0.53	0.38	0.16 (-0.05:0.36)
Cleveland Clinic Florida Incontinence Score (CCFIS)				
CCFIS score†	0 = continent; 20 = total incontinence	-3.06	-2.85	-0.21 (-1.15:0.72)

* Positive value indicates improvement; † Negative value indicate improvement

Patient Counseling Information

The patient should be advised that Solesta treatment is not effective for all patients with fecal incontinence and that repeat treatment might be required for treatment effect. It should also be made clear to the patient that the available clinical study data are not sufficient to predict in whom Solesta treatment will be effective. The patient should be informed about post-treatment care and potential adverse events. The patient should also be made aware that the implants might be detected during future anorectal examinations and radiographic imaging of the pelvis. Patients should be instructed to inform all future treating physicians about the presence of Solesta gel.

If there should be a need for future surgery (e.g., hemorrhoidectomy) the Solesta implant can be resected.

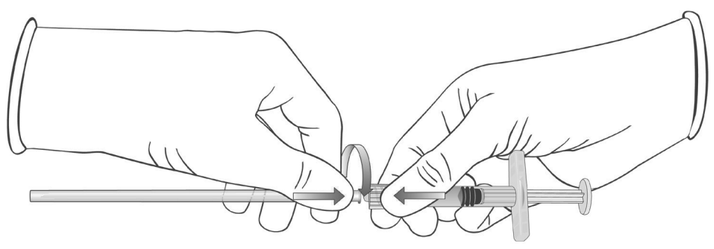
Directions for Use

Solesta should be administered by qualified physicians with experience in the treatment of anorectal conditions and who have successfully completed a comprehensive training and certification program in the Solesta injection procedure. Solesta should only be used after a thorough physical evaluation of the patient to exclude treatable underlying disorders.

For the safe use of Solesta it is important that a new sterile needle is properly assembled and tightly fastened to each syringe.

Please note that the Luer-lock adapter is snapped onto the syringe and held in place with friction only. It can rotate freely or be pulled off should enough force be applied. Because of this it is recommended that the thumb and forefinger be held firmly around the Luer-lock adapter on the glass syringe while attaching the needle to the syringe. DO NOT attach the needle by holding onto the glass barrel of the syringe. To facilitate proper threading/fastening of the needle hub and Luer-lock adapter, please firmly push and rotate the needle hub into the Luer-lock adapter as illustrated in Figure 4.

Figure 4. Proper threading/fastening of the needle hub and Luer-lock adapter



To avoid any interruption in patient treatment or the need to repeat a procedure because of leakage, or accidental contamination or damage of a syringe or needle, it is recommended that extra Solesta cartons be kept in inventory.

Method of Administration

1. The treatment is administered as an outpatient procedure without anesthesia.
2. Prior to treatment, the rectum should be evacuated with an enema. The enema should be given immediately prior to the procedure to ensure evacuation of the anorectum. Additional cleansing of the injection area with an antiseptic may be performed prior to injection.
3. Use of prophylactic antibiotics is recommended.
4. Four Solesta syringes should be made ready with mounted needles under aseptic conditions. Have small swabs and suction prepared and ready for use.
5. The patient is placed in the left lateral position, and a lubricated anoscope is inserted. The obturator is removed and the anoscope withdrawn so that the dentate line is identified.
6. The four injections are to be given in the following order: posterior, left lateral, anterior, and right lateral.
7. The injections should be performed slowly to avoid stress on the Luer-lock connection and allow the tissue to adapt to the injected gel.
8. Under direct vision, the mucosa is penetrated, approximately 5 mm proximal to the dentate line. The needle is advanced a further 5 mm at approximately 30° to the axis of the rectum. If the patient indicates pain at the puncture, the injection site should be adjusted a few mm in the cephalic direction. If the puncture is painless, 1 mL of Solesta is injected in the deep submucosal layer. After injection, the needle should be kept in position for 15-30 seconds to minimize leakage of Solesta.
9. The injection is to be repeated at the remaining three injection sites. A new needle should be used for each syringe and injection site.
10. After completion of the 4 injections, the anoscope is extracted and the patient may rise. The patient should be instructed to rest at the clinic for approximately 60 minutes.
11. If no bleeding or other treatment related symptoms are observed during this time, the patient can be allowed to leave the clinic.
12. Confirming placement of Solesta gel by imaging may be of benefit.

Post-treatment care

1. The patient should be instructed to avoid taking hot baths during the first 24 hours post-treatment.
2. The patient should be informed of the risk of infections and bleeding.
3. The patient should be instructed to contact the clinic or physician's office immediately if symptoms of rectal bleeding, bloody diarrhea, fever, tenesmus or problems with urinating occur.
4. Anti-diarrheal drugs should not be used for one week after treatment.
5. Stool softeners may be used until the first defecation occurs.
6. Analgesics other than Non-steroidal Anti-inflammatory Drugs (NSAIDs) may be prescribed, if needed.
7. The patient should be instructed to:
   - Avoid physical activity for 24 hours
   - Avoid sexual intercourse and strenuous physical activity for one week (e.g., horse back riding, bicycling and jogging, etc.)
   - Avoid anal manipulation for one month (e.g., insertion of suppositories or enemas and rectal temperature recording)

Re-treatment procedure

1. If the patient does not have an adequate response to Solesta after the first injection, a re-injection with a maximum of 4 mL Solesta can be performed, no sooner than 4 weeks after the first injection.
2. The re-treatment procedure and all pretreatment preparations are performed the same way as the initial treatment procedure. All pretreatment preparations and injection procedures should be performed as described in "Methods of Administration" above. However, the point of injection should be made in between the initial injections, shifted one-eighth of a turn (e.g., left posterolateral, left anterolateral, right anterolateral, and right posterolateral).

How Supplied

Solesta is supplied in a glass syringe with a standard Luer-lock fitting containing 1 mL gel. Each syringe is terminally moist heat sterilized in a pouch. Four pouches, each containing one syringe are packed in a carton together with five Sterican needles (21G x 4¾ inches, 0.80 mm x 120 mm), patient record labels and a package insert. The needles are sterilized by ethylene oxide.

Storage

Store at a temperature up to 25°C (77°F) and protect from sunlight and freezing.

For Information

Solesta is marketed by Oceana Therapeutics, Inc. For information or to report adverse events contact:

Oceana Therapeutics, Inc.
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Edison, NJ 08817
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info@oceanathera.com

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