Solesta for the Treatment of Fecal Incontinence

Introduction

Fecal incontinence (FI), loosely defined as the inability to defer the urge to pass stool until a socially acceptable time or place, affects about 19 million Americans.1 FI can be a devastating condition, leading to a decrease in activities of daily living (ADLs) and having an adverse influence on quality of life (QoL) for those with the condition.2,3 Unfortunately, stigma associated with FI often prevents patients from seeking treatment.4 FI has a broad range of causes with surgical and obstetrical trauma being the leading etiologies. In addition, a number of chronic diseases, including obesity, diabetes, and chronic obstructive pulmonary disease have been associated with higher rates of FI.5 Treatment options for patients with FI range from conservative, nonoperative therapies to invasive, surgical procedures. More recently, minimally invasive options have been introduced into the treatment paradigm for patients who have FI.

Burden of FI: Effect on QoL

The devastating influence of FI on the well-being of affected patients is significant and closely correlates with the frequency and severity of episodes. In a study that took into account frequency of FI episodes, amount of stool lost, composition of stool lost, and fecal urgency, 82% of those with severe symptoms had a moderate to severe negative influence on one or more aspects of their QoL.6 The most profound effects may be psychological, with high rates of depression and anxiety reported in those with FI relative to the general population.7 FI also has been shown to affect the ability or willingness of individuals to participate in ADLs.8 In the largest existing assessment of US women with FI, 18.8% of participants (1,096 of 5,817) reported at least one episode of bowel leakage per year.9 Roughly 40% (368 of 938) of women with FI experienced a severe negative influence on QoL in one or more areas of their daily lives, with the most affected areas relating to frustration, and emotional well-being and participation in social activities. The study also found that despite the negative effect on QoL, less than one-third of women with the condition discussed it with their physician.2,9,10 FI imposes considerable social barriers on patients with the disorder.

Epidemiology

Approximately 8% of noninstitutionalized adults in the United States report having experienced at least 1 episode of FI over the past 30 days.9 Although FI rates are relatively higher in women,10 rates of FI increase with age regardless of gender.11 In women, childbirth by vaginal delivery may cause damage to the pelvic floor or other recto-genital structures causing FI soon after delivery, or manifesting several years later.

Evaluation of FI

Evaluation of patients with FI begins with a thorough history, including surgical and obstetric history. The use of intake questionnaires such as the Cleveland Clinic Fecal Incontinence Score (CCFIS) or Fecal Incontinence Severity Index (FISI) are helpful in gauging the extent and severity of the condition.11 Following a history and physical examination, additional evaluation in a comprehensive anorectal physiology lab may be useful. Anorectal manometry, pudendal nerve testing, and endoanal sonography all provide additional information that may be useful in directing therapy.

Treatment Strategies

Although treatment selection is dependent on many variables, conservative, noninvasive therapies are regarded as the first-line approach in most cases of FI.12 Conservative approaches include diet and medical therapies.13 Abstention from foods that increase colonic transit time, such as coffee, or increasing consumption of foods that increase bulk, such as fiber, should be an initial step in treatment.12,13 Additionally, the use of antidiarrheals may be appropriate for slowing transit time.13 In addition to these conservative therapies, pelvic floor exercises using biofeedback may be sufficient in improving bowel control. Although the efficacy of conservative approaches varies, surgical therapies may provide more definitive correction when anatomic defects are the primary cause of incontinence.13 A variety of surgical approaches have been described for specific anatomic defects; however, sphincteroplasty is the most common surgical repair used.10 The benefit from surgery is dependent on selection of the appropriate procedure performed by an experienced team. Even with appropriate patient and procedure selection, the results may not be durable.13

Minimally Invasive Treatment Options for FI

Historically, patients with FI who did not respond to conservative therapies had surgical intervention as their only alternative option, and yet not all patients were candidates for surgery. Recently, however, 2 relatively noninvasive treatments have been introduced into the armamentarium for these patients. Sacral nerve stimulation (SNS) and hyaluronic acid/dextranomer injections (Solesta, Salix Pharmaceuticals) have shown sustained benefit in multicenter trials.14,15 Solesta: An Effective Treatment Option for FI

Solesta injections are a relatively noninvasive, office-based treatment. In 2011, it was approved by the FDA for the treatment of FI on the basis of a multicenter, double-blind, sham-controlled trial.15 Solesta combines dextranomer microspheres with stabilized hyaluronic acid, which is injected into the submucosal layer of the anal canal and serves to augment tissue volume surrounding the sphincter. Four injections are typically performed without anesthesia in a quick, single-in-office procedure.

The safety and efficacy of Solesta was demonstrated in a registration trial of 206 adults with FI who had failed conservative therapy.15 Patients were randomized to receive either dextranomer or sham, and the end point was the percentage of patients with at least a 50% reduction in episodes of FI from baseline.15 After 6 months, 52% of those receiving dextranomer and 31% of those receiving the sham achieved this end point, producing an odds ratio of 2.36 (95% confidence interval, 1.24-4.47; P=0.0089; Figure).15,16 Treatment with Solesta was generally well tolerated by patients. The most common adverse events (>4%) were proctalgia, anorectal hemorrhage, injection site hemorrhage, pyrexia, injection site pain, diarrhea, and anorectal discomfort. There were 2 cases of rectal abscess and 1 case of Escherichia coli bacteremia, and all were successfully resolved.15

The 47.2% reduction in the median number of FI episodes during 2 weeks of treatment with dextranomer and the 79.5% increase in the mean number of incontinence-free days at 12 months were statistically significant (P<0.0001 for both). Furthermore, significant improvements in QoL scores at 12 months were achieved by patients treated with Solesta for the 4 measured domains (lifestyle, coping and behavior, depression and self-perception, and embarrassment).15

Patients should be instructed to avoid physical activity for 24 hours after treatment with Solesta and to avoid sexual intercourse and strenuous physical activity for one week (eg, horseback riding, bicycling, and jogging). If a 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 treatment.

Conclusion

FI is an underrecognized but common disorder that is a source of significant patient distress. Stigma may influence a patient’s decision not to seek treatment despite the significant burden of FI, poor QoL, and restricted ADLs. Although surgery may be an appropriate intervention in complex cases, minimally invasive approaches may provide adequate symptom control with a low risk for complications. Solesta, a quick, in-office procedure performed without the need for anesthesia, may be a viable solution for patients suffering from FI. Clinical data has shown that Solesta provides dependable results through 36 months, including a significant reduction in FI episodes in as few as 3 months, as well as meaningful improvements in QoL.

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; rectocoele; rectal varices; presence of existing implant (other than Solesta) in the anorectal region; and allergy to hyaluronic acid–based products.

Please see Brief Summary of Prescribing Information on adjacent page.

References


Disclosure: Dr. Bernstein reported that he is on the speaker’s bureau for Salix.
Solesta®

Brief Summary

Please consult Package Insert for full prescribing information.

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).

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: abscesses, 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 antibiotic 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 occurs at the site of injection.
- 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 should 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 fissing, anal hemorrhage, anal prolapse, anal pruritus, anorectal discomfort, back pain, constipation, C-reactive protein increased, chill, cold sweat, defecation urgency, dermatitis, diarrhea, device dislocation, dizziness, dyspnea, dyspepsia, escherichia bacteria, fecal incontinence, feces hard, fatigue, gastrointestinal motility disorder, gastrointestinal pain, genital discharge, genital prolapse, hematoclastia, hematopsia, hemorrhoids, infection, injection site abscess, injection site discomfort, injection site hernomage, 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, malabsorption, mucosal erosion, mucosal ulceration, pain, perianal abscess, perineal pain, procititsa, proctitis, pyrexia, rectal abscess, rectal discharge, rectal hemorrhage, rectal lesion, rectal obstruction, rectal prolapse, rectal spasm, rectal tenesmus, rectovaginal septum abscesses, 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.

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 solest cohort of all 206 patients treated in the Pivotal study with either Solesta or Sham. Safety data for Solesta are available from 358 patients in 197 total patients followed for up to 18 months post-treatment (i.e., 130 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 were reported 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 bacteraemia, 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 air anal proplase, one (1) case of lancing of a hemorrhoid, and one (1) case of a Kansoing in a pre-existing anal lacer. 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.

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., proctectomy) 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 examination 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.

- 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.
- Anti-diarrheal drugs should not be used for one week after treatment.
- Stool softeners may be used until the first defecation occurs.
- Analgesics other than Non-steroidal Anti-inflammatory Drugs (NSAIDs) may be prescribed, if needed.

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 a 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, shifed one-eighth of a turn (e.g., left posterior lateral, right anterolateral, right posterior lateral).

How Supplied

Solesta is supplied in a glass syringe with a standard Luer-lock fitting containing 1 ml gel. Each syringe is terminally heat sterilized in a pouch. Four pouches, each containing one syringe are packed in a carton together with five Sterican needles (210 x 4 inches, 0.60 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.

To report adverse events, a product complaint, or for additional information, call 1-800-558-0024. Solesta is under license from and manufactured by B-Med AB for Salix Pharmaceuticals, Inc. Solesta is registered trademark of Galderma S.A.