Injectable bulking agents — fecal incontinence

Clinical Policy ID: CCP.1168

Recent review date: 7/2021

Next review date: 11/2022

Policy contains: Durasphere; fecal incontinence; non-animal stabilized hyaluronic acid/dextranomer; pelvic floor dysfunction; Solesta.

This policy is a Sandhills Center Clinical Coverage Policy adopted from AmeriHealth Caritas of North Carolina. These clinical policies are used to assist with making coverage determinations. Sandhills Center's clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by Sandhills Center when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. Sandhills Center clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Sandhills Center's clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Sandhills Center will update its clinical policies as necessary. Sandhills Center clinical policies are not guarantees of payment.

Coverage policy

Injectable bulking agents for fecal incontinence are investigational/not clinically proven and, therefore, not medically necessary.

Limitations

Other uses of injectable bulking agents may be medically necessary for other gastro-urinary indications, such as urinary incontinence.

Alternative covered services

- Biofeedback.
- Bladder or bowel training.
- Dietary management.
- Electrical stimulation.
- Pelvic floor muscle training.
- Pharmacotherapy.

- Surgery (e.g., post-anal repair, sphincteroplasty, artificial anal sphincter implantation, total pelvic floor repair, or bowel diversion).

Background

Fecal incontinence, also called anal incontinence or accidental bowel leakage, is loss of control of the bowels resulting in involuntary loss of liquid or solid feces, or flatus, from the rectum. Fecal incontinence is a symptom of an extensive list of underlying causes. The prevalence of fecal incontinence ranges from 7% to 15% in community-dwelling men and women and may be higher in institutionalized patients (Bharucha, 2015). Fecal incontinence has a negative impact on activities of daily living and quality of life and is associated with a substantial economic burden, particularly in patients who require surgical therapy (Bharucha, 2015).

The strongest independent risk factors for fecal incontinence in community populations are bowel disturbances such as diarrhea, the symptom of rectal urgency, trauma, and burden of chronic illness (Bharucha, 2015; Norton, 2007). The pathophysiological mechanisms responsible for fecal incontinence include diarrhea, anal and pelvic floor weakness, reduced rectal compliance, and reduced or increased rectal sensation; many patients have multifaceted anorectal dysfunctions. The type (urge, passive, or combined), etiology (anorectal disturbance, bowel symptoms, or both), and severity classify the symptom (Bharucha, 2015). Diagnosis encompasses a detailed medical history, physical exam, and a range of tests to assess the structure and function of the rectum, anus, and pelvic floor muscles (National Institute of Diabetes and Digestive and Kidney Diseases, 2021).

Current treatments for fecal incontinence range from conservative medical therapy aimed at reducing symptoms to surgical interventions intended to correct anal sphincter or pelvic floor abnormalities. Injectable perianal bulking agents have emerged as potential minimally invasive treatment alternative following their reported success in treating urinary incontinence (Wald, 2014). A biocompatible material is injected into the anal submucosa or intersphincteric space to close the anal canal or raise the pressure inside the anal canal to avoid fecal incontinence. Typically, a colorectal surgeon or gastroenterologist performs the procedure under local anesthesia, and the procedure may be done in an outpatient clinic setting. The simplicity and minimal invasiveness of this procedure make it an attractive treatment alternative for fecal incontinence.

Several different materials have been used to treat urinary incontinence, but to date, the U.S. Food and Drug Administration (2011) has approved only one bulking agent for treatment of fecal incontinence: dextranomer in stabilized sodium hyaluronate, also known as non-animal stabilized hyaluronic acid/dextranomer in stabilized hyaluronic acid or NASHA Dx, marketed under the trade name Solesta® (Q-Med AB, Sweden for Salix Pharmaceuticals, Inc., Raleigh, North Carolina) as a class III medical device 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). It 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.
- Patients who were pregnant, breast feeding, or without adequate contraception within the first year, or within one year postpartum.
- Presence of existing implant (other than Solesta) in the anorectal region.

- Allergy to hyaluronic acid-based products.

As a condition of approval, The U.S. Food and Drug Administration (2011) requires the manufacturer to provide data regarding numbers of devices sold and distributed with necessary context to ascertain the frequency and prevalence of adverse events, and mandates two additional studies to assess the long-term safety and durability of Solesta:

- A single-arm, multicenter observational study of safety and durability through 36 months.
- A substudy to show the anatomic stability of Solesta in at least 30 subjects by comparing anatomical positioning via transrectal ultrasonography at time of injection to positioning at six and 36 months.

Findings

We identified a systematic review (Maeda, 2013), one cost-effectiveness analysis (Bernstein, 2014) and two evidence-based guidelines (National Institute for Health and Care Excellence, 2007; Wald, 2014) for this policy. The overall quality of the evidence is low given the scarcity of controlled studies and high risk of bias among uncontrolled studies. Methodological limitations of the uncontrolled studies included small sample sizes, lack of blinding, and high numbers of dropouts.

The majority of studies evaluated Solesta for treating fecal incontinence. The evidence consists of one randomized controlled trial comparing Solesta to sham controls (the PIVOTAL study; clinicaltrials.gov identifier NCT00605826), one randomized controlled trial comparing Solesta to anal sphincter training with biofeedback (clinicaltrials.gov identifier NCT00303030), and several small uncontrolled studies using Solesta and other bulking agents. The Pivotal Study is the primary data set that demonstrated the safety and effectiveness of Solesta, along with supporting evidence of safety and effectiveness from one uncontrolled, multisite open-label study (clinicaltrials.gov identifier NCT01110681) and one single-site, proof-of-concept study (clinicaltrials.gov identifier NCT01380132). All but one of the Solesta studies were industry sponsored.

The study populations comprised patients with fecal incontinence who had not responded to conservative treatment (21 to 206 patients per study). All patients received four injections of 1 mL of Solesta in each quadrant of the anal submucosa. Patients were generally discharged from the treatment setting after a brief period of observation. After one month, patients without improvement of symptoms were offered a second treatment. Efficacy endpoints included the change in the number of incontinence episodes. A significant treatment response was defined as a 50% or greater decrease in fecal incontinence episode frequency compared with baseline, the number of incontinence-free days and changes in incontinence scores using validated instruments. Patients recorded fecal incontinence episodes and patterns in diaries when warranted. The duration of follow-up ranged from three months to three years.

The evidence is insufficient to support the use of injectable bulking agents for treatment of fecal incontinence in adults. A limited number of uncontrolled studies of bulking agents other than Solesta are insufficient to permit conclusions regarding their safety and efficacy for fecal incontinence. The results for Solesta suggest the procedure was well tolerated, with the majority of treatment-related adverse events considered mild or moderate in intensity. These included mild or moderate pain or discomfort in the rectum or anus, minor to moderate bleeding or spotting from the rectum, fever, abdominal pain, diarrhea, and constipation after treatment.

Solesta is associated with some modest but statistically significant symptomatic improvements and may be a cost-effective alternative up to three years of follow-up in persons who have not responded to conservative treatment. However, improvement in many incontinence scores and general health was not statistically significant, and it is unclear if improvement in incontinence scores correlated with practical symptom improvements that mattered to the patients. Results of the sham-controlled study suggest a significant placebo effect, and the other controlled study suggested comparable results between Solesta and anal sphincter training

with biofeedback.

Additional research is needed to determine the clinical value of bulking agents for fecal incontinence. Given the large placebo effect observed, larger, independent, randomized, sham-controlled studies are needed to further evaluate the efficacy, durability, and safety of this treatment. Future studies should compare Solesta with standard therapies such as sacral nerve stimulation and other minimally invasive alternatives. There is also a need to better define the patient selection criteria by examining variables that predict which patients will derive the most clinical benefit from this therapy. To fulfill FDA conditions for continued approval, one observational study is underway to evaluate the long-term safety and effectiveness of Solesta through three years in a real-world setting (clinicaltrials.gov identifier NCT01647906).

According to a horizon scanning report, tissue-bulking agents have potential to improve health outcomes, but would not always completely resolve fecal incontinence (ECRI Institute, 2012). Those with muscle disruptions will probably need surgery. The intervention might become widely accepted because it is a noninvasive alternative to surgery that would appeal to patients, but most experts wanted to see additional trial results. Similarly, evidence-based guidelines confirmed the potential of bulking agents for treating fecal incontinence in patients who are refractory to conservative therapy, but further studies are needed (National Institute for Health and Care Excellence, 2007; Wald, 2014).

In 2016, we found one new evidence-based guideline by the American Society of Colon and Rectal Surgeons for treatment of fecal incontinence (Paquette, 2015). They issued a weak recommendation for injection of biocompatible bulking agents into the anal canal to help decrease episodes of passive fecal incontinence. Their recommendation was based on limited, moderate-quality evidence showing modest improvements in short-term outcomes, although long-term follow-up with regard to safety and efficacy awaits further experience.

The Agency for Healthcare Research and Quality conducted a comprehensive systematic review of surgical and nonsurgical treatments for fecal incontinence (Forte, 2016). Low-quality evidence at six months' follow-up suggests dextranomer anal bulking injections are more effective than sham injections on outcome measures of quality of life, the number of fecal incontinence-free days, and the percent of adults with at least 50% reduction from baseline in fecal incontinence episodes. They are not more effective than pelvic floor muscle training plus biofeedback with or without electrostimulation on measures of fecal incontinence severity and quality of life, and not more effective than sham injection on fecal incontinence severity or episode frequency.

Moderate-quality evidence suggests another injectable bulking agent Durasphere® (Coloplast Corp., Minneapolis, Minnesota), which is approved for stress urinary incontinence and represents an off-label use for fecal incontinence, reduced fecal incontinence severity for up to six months, but gains diminished thereafter. The authors stress that there is little high-quality evidence to guide decisions about the optimal surgical or nonsurgical treatment options for fecal incontinence beyond standard care (i.e., dietary fiber supplements or stool-modifying drugs). These findings do not change earlier conclusions. Therefore, no changes to the policy are warranted.

In 2018, we added no new information to add that would materially change the policy.

In 2019, we added two systematic reviews (Lal, 2019; Simillis, 2019) to the policy with no material changes to coverage. The policy ID was changed from CP# 08.02.04 to CCP.1168.

In 2020, we identified no newly published, relevant literature to add to the policy.

In 2021, we identified no newly published, relevant literature to add to the policy.

References

On March 31, 2021, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the

Centers for Medicare & Medicaid Services. Search terms were “fecal incontinence (MeSH),” “bulking agent,” “NASHA,” and “dextranomer.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

5/2015: initial review date and clinical policy effective date: 10/2015

7/2016: Policy references updated.

7/2017: Policy references updated.

7/2018: Policy references updated.

7/2019: Policy references updated. Policy ID changed.

7/2020: Policy references updated.