Injectable bulking agents — fecal incontinence

Clinical Policy ID: CCP.1168

Recent review date: 7/2024

Next review date: 11/2025

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

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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, quality of life and is associated with a substantial economic burden, particularly in patients who require surgical therapy. For those who fail initial options, the remaining choices are pelvic floor biofeedback, perianal bulking agent injections, and sacral nerve stimulation that have not been compared with each other (Bharucha, 2021).

The strongest independent risk factors for fecal incontinence in community populations are bowel disturbances such as diarrhea, the symptom of rectal urgency, trauma, and chronic illness (Bharucha, 2015). 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 symptoms experienced (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, 2023).

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 and cost of this procedure make it an attractive treatment alternative for fecal incontinence (Bharucha, 2021).

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

Clinical Guidelines

The National Institute for Health and Care Excellence (2007), Wald (2014), the American Society of Colon and Rectal Surgeons (Paquette, 2015), and European professional medical societies (Assmann, 2022) confirm the potential of injectable bulking agents for treating fecal incontinence in patients who are refractory to conservative therapy. The American Society of Colon and Rectal Surgeons issued a weak recommendation for injection of biocompatible bulking agents into the anal canal to help decrease episodes of passive fecal incontinence, based on limited, moderate-quality evidence showing modest improvements in short-term outcomes. European professional medical societies recommend injectable bulking agents as one first-line treatment for fecal incontinence, based on a low level of evidence, for patients with loose stools and personalized based on patient responses. However, these guidelines also emphasize the need for further studies to establish the efficacy and safety of these treatments.

Systematic Reviews

Several systematic reviews and meta-analyses have been conducted on the use of injectable bulking agents for fecal incontinence. Maeda (2013) conducted a systematic review, while the Agency for Healthcare Research and Quality (Forte, 2016) conducted a comprehensive systematic review of surgical and nonsurgical treatments for fecal incontinence. The latter found low-quality evidence at six months' follow-up suggesting that 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 episodes. However, 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. Hong (2017) found that administration of injectable bulking agents has demonstrated significant improvement midterm, but further research is needed to improve the quality of the evidence.

A separate systematic review that looked at eight studies (n = 166) with a goal of comparing outcomes of self-expanding implantable bulking agents with non-self-expandable injectable bulking agents. No comparison was possible due to lack of controlled studies of injectable agents (Gassner, 2022).

A systematic review encompassing 16 nonrandomized studies (n= 420) patients investigated the efficacy of conventional injectable bulking agents, including carbon, Teflon, silicon, collagen, and autologous fat, for the treatment of passive fecal incontinence (Dexter, 2024). The review revealed limited evidence supporting their effectiveness, with only two studies demonstrating improvement exceeding 50%, while the remaining studies reported improvements ranging from 15% to 50% at long-term follow-up assessments. Complications affected up to 10% of patients, and side effects were observed in up to 12% of cases (Dexter, 2024). A more recent

material, non-animal stabilized hyaluronic acid/dextranomer, initially exhibited promising results in a randomized, placebo-controlled trial involving 206 patients. In this trial, more than 50% improvement was observed in 53.2% of the intervention group, compared to 30.7% in the sham group. However, the complete continence rate at six months was only 6%, and concerns regarding the durability, cost, and uncertain patient selection criteria have hindered its widespread adoption (Dexter, 2024).

Other Forms of Evidence

A cost-effectiveness analysis by Bernstein (2014) evaluated Solesta for treating fecal incontinence. Other forms of evidence include the PIVOTAL study (NCT00605826) and another randomized controlled trial (NCT00303030), which evaluated Solesta for treating fecal incontinence, as well as 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 (NCT01110681) and one single-site, proof-of-concept study (NCT01380132). All but one of the Solesta studies were industry sponsored. These studies had methodological limitations, including small sample sizes, lack of blinding, and high numbers of dropouts.

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, with a significant treatment response 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 results for Solesta suggest the procedure was well tolerated, with the majority of treatment-related adverse events considered mild or moderate in intensity, including 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.

A horizon scanning report (ECRI Institute, 2012) suggested that tissue-bulking agents have potential to improve health outcomes but would not always completely resolve fecal incontinence. 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.

Lal (2019) found moderate-quality evidence suggesting 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.

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.

In 2022, we added a current European consortium guideline algorithm (Assmann, 2022), relevant to the policy, with no material changes to coverage.

In 2023, we added a systematic review (Gassner, 2022) that compared outcomes of self-expanding implantable bulking agents with non-self-expandable injectable bulking agents.

In 2024, we reorganized the findings section to more clearly delineate between evidence types (i.e., clinical guidelines, systematic reviews, other forms of evidence, and we added a new systematic review that examined effectiveness and safety of injectable bulking agents for the treatment of passive fecal incontinence (Dexter, 2024). No policy changes warranted.

References

On June 6, 2024, 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

4/2015: initial review date and clinical policy effective date: 9/2015

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.

7/2021: Policy references updated.

7/2022: Policy references updated.

7/2023: Policy references updated.

7/2024: Policy references updated.