Policy Number	**SUR710.008**
Policy Effective Date	**12/15/2025**

Injectable Bulking Agents for the Treatment of Urinary and Fecal Incontinence

Table of Contents
Coverage
Policy Guidelines
Description
Rationale
Coding
References
Policy History

Related Policies (if applicable)
None

Disclaimer

Carefully check state regulations and/or the member contract.
Each benefit plan, summary plan description or contract defines which services are covered, which services are excluded, and which services are subject to dollar caps or other limitations, conditions or exclusions. Members and their providers have the responsibility for consulting the member's benefit plan, summary plan description or contract to determine if there are any exclusions or other benefit limitations applicable to this service or supply. **If there is a discrepancy between a Medical Policy and a member's benefit plan, summary plan description or contract, the benefit plan, summary plan description or contract will govern.**

Coverage

The use of carbon-coated spheres, calcium hydroxylapatite, polyacrylamide hydrogel, or polydimethylsiloxane **may be considered medically necessary** to treat stress urinary incontinence in men and women who have failed appropriate conservative therapy (see Policy Guidelines).

Individuals whose incontinence does not improve after five treatment procedures are considered treatment failures and additional treatment procedures **are considered not medically necessary**.

The use of autologous cellular therapy (e.g., myoblasts, fibroblasts, muscle-derived stem cells, adipose-derived stem cells), autologous fat, and autologous ear chondrocytes to treat stress urinary incontinence **is considered experimental, investigational and/or unproven**.

The use of any other periurethral bulking agent, including, but not limited to Teflon, to treat stress urinary incontinence **is considered experimental, investigational and/or unproven**.

The use of periurethral bulking agents to treat urge urinary incontinence **is considered experimental, investigational and/or unproven.**

The use of perianal bulking agents to treat fecal incontinence **is considered experimental, investigational and/or unproven.**

Policy Guidelines

Individuals should have had an inadequate response to conservative therapy or therapies; in general, these treatments should have been used for at least 3 months. Conservative therapy for stress incontinence includes pelvic floor muscle exercises and behavioral changes, such as fluid management and moderation of physical activities that provoke incontinence. Additional options include intravaginal estrogen therapy, use of a pessary, and treatment of other underlying causes of incontinence in individuals amenable to these treatments.

Description

Bulking agents are injectable substances used to increase tissue bulk. They can be injected periurethrally to treat urinary incontinence and perianally to treat fecal incontinence. The U.S. Food and Drug Administration (FDA) has approved several bulking agent products for treating urinary incontinence and one for treating fecal incontinence.

Incontinence
Incontinence, especially urinary, is a common condition and can have a substantial impact on quality of life. Estimates from the National Center for Health Statistics have suggested that among noninstitutionalized persons 65 years of age and older, 44% have reported issues with urinary incontinence and 17% issues with fecal incontinence. (1)

Treatment
Urinary Incontinence
Injectable bulking agents are space-filling substances used to increase tissue bulk. When used to treat stress urinary incontinence (SUI), bulking agents are injected periurethrally to increase tissue bulk and thereby increase resistance to the outflow of urine. The bulking agent is injected into the periurethral tissue as a liquid that solidifies into a spongy material to bulk the urethral wall. Bulking agents may be injected over a course of several treatments until the desired effect is achieved. Periurethral bulking agents have been widely used for incontinence in women. Men have also been treated, typically those with postprostatectomy incontinence.

Key factors in determining the optimal product are biocompatibility, durability, and absence of migration. A number of periurethral bulking agents to treat urinary incontinence have been cleared for marketing by the U.S. Food and Drug Administration (FDA); however, products developed to date have not necessarily met all criteria of the ideal bulking agents. The first FDA

approved product was cross-linked collagen (e.g., Contigen). The agent was found to be absorbed over time and symptoms could recur, requiring additional injections. Contigen production was discontinued in 2011. Other periurethral bulking agents cleared by FDA for urinary incontinence include carbon-coated beads (e.g., Durasphere), spherical particles of calcium hydroxylapatite (CaHA®) in a gel carrier (Coaptite®), polydimethylsiloxane (silicone, Macroplastique®), cross-linked polyacrylamide hydrogel (Bulkamid®), and ethylene vinyl alcohol copolymer implants (e.g., Tegress®, formerly Uryx®). Tegress was voluntarily removed from the market due to safety concerns.

Fecal Incontinence

After the success of periurethral bulking agents for treating SUI, bulking agents injected into the anal canal have been proposed to treat fecal incontinence. In particular, bulking agents are a potential treatment for passive fecal incontinence associated with internal anal sphincter dysfunction. The bulking agent is injected into the submucosa of the anal canal to increase tissue bulk in the area, which narrows the opening of the anus. Current treatment options for fecal incontinence include conservative measures (e.g., dietary changes, pharmacotherapy, pelvic floor muscle exercises), sacral nerve stimulation, and surgical interventions to correct an underlying problem.

Several agents identical or similar to those used for urinary incontinence (e.g., Durasphere, silicone biomaterial) have been studied for the treatment of fecal incontinence. To date, only 1 bulking agent has been approved by the FDA for fecal incontinence. This formulation is a non-animal-stabilized hyaluronic acid/dextranomer in stabilized hyaluronic acid (NASHA Dx), marketed by Palette Life Sciences as Solesta. A hyaluronic acid/dextranomer formulation (Deflux®) from the same company has been commercially available for a number of years for the treatment of vesicoureteral reflux in children (see medical policy SUR710.022 on the treatment of vesicoureteral reflux with bulking agents).

Autologous fat and autologous ear chondrocytes have also been used as periurethral bulking agents; autologous substances do not require FDA approval. Polytetrafluoroethylene (Teflon®) has been investigated as an implant material but does not have FDA approval. A more recently explored alternative is cellular therapy with myoblasts, fibroblasts, or stem cells (muscle-derived or adipose-derived). In addition to their use as periurethral bulking agents, it has been hypothesized that transplanted stem cells would undergo self-renewal and multipotent differentiation, which could result in the regeneration of the sphincter and its neural connections.

Regulatory Status

Several periurethral bulking agents have been approved by FDA through the premarket approval process for the treatment of SUI due to intrinsic sphincter deficiency; other than Contigen®, approval is only for use in adult women. Products include:

- In 1993, Contigen (Allergan), a cross-linked collagen, was approved. A supplemental approval in 2009 limited the device's indication to the treatment of urinary incontinence due to intrinsic sphincter deficiency in patients (men or women) who have shown no

improvement in incontinence for at least 12 months. Allergan ceased production in 2011; no reason for discontinuation was provided publicly.

- In 1999, Durasphere (Advanced UroScience), a pyrolytic carbon-coated zirconium oxide sphere, was approved.
- In 2004, Uryx (CR Bard), a vinyl alcohol copolymer implant, was approved. In 2005, approval was given to market the device under the name Tegress. In 2007, Tegress® was voluntarily removed from the market due to safety concerns.
- In 2005, Coaptite (Boston Scientific, previously BioForm Medical and Merz Aesthetics), spherical particles of calcium hydroxylapatite, suspended in a gel carrier, was approved.
- In 2006, Macroplastique (Laborie, previously Cogentix Medical), polydimethylsiloxane, was approved.
- In 2020, Bulkamid Urethral Bulking System (Axonics Modulation Technologies, Inc.), a soft hydrogel that consists of 97.5% water and 2.5% polyacrylamide, was approved.
- In 2011, NASHA Dx, marketed as Solesta (Q-Med now Palette Life Sciences), was approved by FDA through the premarket approval process as a bulking agent to treat fecal incontinence in patients 18 years and older who have failed conservative therapy. FDA product code: LNM.

Rationale

Medical policies assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent 1 or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. Randomized controlled trials are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Stress Urinary Incontinence

Clinical Context and Therapy Purpose

The purpose of injectable bulking agents in individuals who have stress urinary incontinence (SUI) is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this policy.

Populations
The relevant population of interest is individuals with SUI.

Interventions
The therapy being considered is injectable bulking agents.

Comparators
The following therapies are currently being used to make decisions about SUI: conservative therapy, other injectable bulking agents, and surgery.

Although Contigen is no longer commercially available, it continues to be a common and acceptable comparator for subsequently developed injectable bulking agents. Previously, a clinical practice guideline (1996) for urinary continence in adults concluded that periurethral collagen is curative in 32% of men and 62% of women. (2) Additionally, an RCT by Corcos et al. (2005) (3) compared the efficacy of collagen injections with surgery in 133 women and found 12-month success rates for collagen treatment (53%) were lower than for surgery (72%), but the collagen-treated group had significantly fewer adverse events (36% vs 63%, respectively).

Outcomes
The general outcomes of interest are symptom reduction, symptom recurrence, and treatment-related adverse events (e.g., pain, infection). Bulking agents may or may not be curative, and follow-up injections may be necessary within 6 months. Beneficial effects may last between 3 and 12 months.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews
Hoe et al. (2021) completed a systematic review that compared the efficacy and safety of all urethral bulking agents for the treatment of women with SUI. (4) The review included 56 articles. Since there was substantial heterogeneity of patient cohorts across studies and

variability in outcomes reported, only a qualitative data analysis was performed. Overall, the authors concluded that the data support the use of Bulkamid and Macroplastique for the treatment of SUI with a short-term efficacy of 30% to 90% and 40% to 85%, respectively. Long-term efficacy for these bulking agents is 42% to 70% and 21% to 80%, respectively. Of all available bulking agents, Bulkamid appears to have the more favorable safety profile, with no cases of erosion or migration associated with its use. Of note, direct comparisons of the urethral bulking agents have not been performed.

Pivazyan et al. (2021) assessed the efficacy and safety of bulking agents compared to surgical methods for the management of women with SUI, with 6 studies included in the final analysis. (5) The included studies (N=710) had 288 women receiving a urethral bulking agent and 317 undergoing a surgical procedure (e.g., midurethral sling, retropubic tape, tension-free vaginal tape). Results revealed bulking agents to be less effective than surgical procedures with regard to subjective improvement after treatment (risk ratio: 0.70; 95% confidence interval [CI], 0.53 to 0.92, p=.01) with no difference between the 2 interventions regarding post-intervention complications (risk ratio: 1.30; 95% CI, 0.30 to 5.66; p=.73).

A Cochrane review by Kirchin et al. (2017) evaluating periurethral bulking agents for urinary incontinence in women identified 14 RCTs (sample ranges, 30 to 355 patients) that included bulking agents in at least 1 study arm. (6) This review updated a 2012 review. (7) All trials included women with a urodynamic diagnosis of stress incontinence, and 7 trials limited eligibility to stress incontinence due to intrinsic sphincter deficiency. The trials varied by types of bulking agent and comparator interventions used. Eight studies compared 2 bulking agents, 2 compared bulking agents with surgery, 1 compared a bulking agent with pelvic floor exercise, and 1 used a placebo comparison group. Several studies required that women had experienced incontinence for a specified period of time (e.g., 6 or 12 months) and/or had already used conservative therapy; 1 study further specified that conservative therapy had to have been used for at least 3 months. Reviewers determined that the data were unsuitable for pooling due to heterogeneity across trials. They concluded that there was insufficient evidence to guide practice and recommended that additional RCTs with a placebo group or conservative treatment arm be conducted.

A systematic review by Davila (2011) identified 20 studies meeting inclusion criteria (prospective clinical studies or RCTs conducted among women with SUI and published in English). (8) Nine studies (n=682 patients) evaluated the bulking agent, cross-linked collagen. Rates of patients considered cured or improved in individual studies ranged from 21% to 81% at 12 months, 7% to 52% at 2 years, and 30% to 43% at more than 4 years. Eight trials (n=507 patients) used cross-linked polydimethylsiloxane injection. Cure rates ranged from 20% to 71% at 12 months and 18% to 40% at long-term follow-up (to 60 months). Reviewers concluded that bulking agents had demonstrated effectiveness at 1 year, but results, particularly with older agents, diminished over time and required repeated injections to restore or enhance improvement.

U.S. Food and Drug Administration-Approved Bulking Agents

Carbon-Coated Beads (e.g., Durasphere)
A double-blind, RCT comparing carbon-coated beads with cross-linked collagen was reported by Lightner et al. (2001) as part of the U.S. Food and Drug Administration (FDA) approval process for Durasphere. (9) The trial found no difference in efficacy or in the number of treatments between groups, although the trial duration (12 months) might not have been sufficient to assess comparative durability.

Calcium Hydroxylapatite (e.g., Coaptite)
Calcium hydroxylapatite (Coaptite) received FDA approval based partly on results from a single-blind, randomized, noninferiority comparison of collagen products among women with SUI. This trial was later published by Mayer et al. (2007) and reported on 231 (78%) of 296 enrolled women. (10) For the primary outcome measure, 83 (63%) patients treated with calcium hydroxylapatite, and 57 (57%) control patients treated with collagen showed an improvement of 1 grade or more on the 4-grade Stamey Urinary Incontinence Scale at 12-month follow-up. Similar results were obtained by an intention-to-treat analysis, with noninferiority of calcium hydroxylapatite to collagen for improvement of at least 1 Stamey grade (58% vs. 51%, respectively) and decrease in pad weight (51% vs. 38%, respectively) of 50% or more.

Polyacrylamide Hydrogel (e.g., Bulkamid)
Polyacrylamide hydrogel (Bulkamid; Contura International A/S) is a gel containing 2.5% cross-linked polyacrylamide and 97.5% apyrogenic water. Sokol et al. (2014) reported on an RCT performed under an FDA-regulated investigational device exemption. (11) This single-blind, multicenter, randomized, noninferiority trial compared Bulkamid with collagen gel (Contigen) in 345 women from 33 study sites in the U.S. and Canada. Up to 3 injections were given. Patients had failed at least 2 previous non-invasive therapies for 3 months each (e.g., behavioral modification, electrical stimulation, pelvic muscle exercise, biofeedback, and/or drug therapy). Patients completed the outcome measures at 1, 3, 6, 9, and 12 months after the last bulking procedure. The primary outcome measure was the responder rate at 12 months, determined by a composite of a 50% decrease in leakage, as measured by the 24-hour pad test, and a minimum 50% decrease in self-reported daily incontinence episodes. Similar rates of patients completed the study (87.8% vs. 87.9%). Bulkamid met the noninferiority margin, with a minimum 50% decrease in leakage and incontinence episodes in 45.9% of patients in the hydrogel group and 41.4% of patients in the collagen gel group according to the intention-to-treat analysis. At 12 months, 47% of patients treated with hydrogel and 50% of patients treated with collagen gel reported no stress incontinence episodes. Urinary Incontinence Quality of Life Scale scores improved similarly in both groups (+31.4 vs +26.3 points; p-value not reported). A treatment-related serious adverse event occurred in a single patient in the Bulkamid group and involved an episode of transient hematuria. A possible study design and conduct limitation is that bias due to inadequate allocation concealment cannot be ruled out as methods were not described.

Itkonen Freitas et al. (2020) evaluated whether Bulkamid is noninferior to tension-free vaginal tape in 224 women with primary SUI not responsive to conservative treatment recruited between September 2015 and March 2017. (12) Enrollees were randomly assigned to tension-

free vaginal tape (n=111) or Bulkamid (n=113). The primary outcome was patient treatment satisfaction as measured on a visual analogue scale with 0 representing extremely unsatisfied and 100 extremely satisfied. This outcome was measured at postoperative visits and a patient satisfaction score ≥80 was defined as a good satisfaction rating. In the Bulkamid group, 46 (43%) women requested additional injection at the 3-month visit while 11 (10%) women did not request additional Bulkamid but preferred to receive tension-free vaginal tape. An additional 5 women eventually underwent tension-free vaginal tape after 2 Bulkamid treatments. In the tension-free vaginal tape group, 2 (2%) women underwent Bulkamid treatment with none undergoing a repeat tension-free vaginal tape procedure. Results revealed that the primary patient satisfaction outcome was achieved by more patients in the tension-free vaginal tape group as compared to the Bulkamid group (96 vs. 64). Bulkamid therapy did not attain the noninferiority threshold set in the study (difference: 35.2%; 95% CI, 24.4 to 45.1, p<.001). Objective cure via the cough stress test was also better in the tension-free vaginal tape group as compared to Bulkamid (95% vs 66.4%; difference: 28.6%; 95% CI, 18.4 to 38.5). Additionally, more women who underwent tension-free vaginal tape would choose the therapy again or recommend it to a friend. The majority of perioperative complications and all reoperations due to complications were associated with tension-free vaginal tape surgery.

Several case series conducted in Europe have been published. The largest (N=256) is by Pai and Al-Singary (2015). (13) Women with stress or mixed urinary incontinence (>1 episode per 24 hours) who received injections of Bulkamid were assessed yearly with quality of life measured by visual analog scale and incontinence by the International Consultation on Incontinence Questionnaire. The primary outcome was whether patients were completely dry (cured) or leaked once a week or less (significant improvement). At the 3-month follow-up, 110 (42.9%) were cured and 102 (39.8%) patients reported significant improvement. These percentages were maintained for 5 years (median, 38 months). However, only 60 (23.4%) patients were available for follow-up at 60 months, limiting interpretation of the long-term results.

A multicenter series by Lose et al. (2010) included 135 adult women with symptomatic stress (n=67) or mixed (n=68) incontinence. (14) Eligibility included the presence of symptoms for at least 12 months, including at least 1 episode of incontinence daily. Ninety-eight (73%) patients completed 12-month follow-up. The primary outcome was response to treatment, defined as patients self-reporting that they considered themselves "improved" or "cured." The response rate was 71% at 6 months and 66% at 12 months. Corresponding cure rates were 16% and 24%. There were 32 treatment-related adverse effects including 2 cases of urinary retention requiring hospitalization and 10 cases of urinary tract infection.

A 2-center prospective series by Maggiore et al. (2013) included 82 women who had had stress incontinence for at least 12 months. (15) Patients received an injection of Bulkamid, and nonresponders were offered a second injection after 3 months. A total of 80 (98%) women were evaluated at 3 and 6 months, and 78 (95%) completed a 1-year follow-up. The primary efficacy outcome was the subjective success rate at 1 year, defined as answering 1 or 2 on the Patient Global Improvement Impression questionnaire, which is scored from 1 (very much better) to 7 (very much worse). In an intention-to-treat analysis, the subjective success rate at 1

year was 74% (61/82 patients). Seven patients reported no change, and none reported symptom worsening. At 1 year, 87% (71/78) of patients were considered to be responders (answer of 1, 2 or 3 on the Patient Global Improvement Impression). Twenty-one (26%) patients had adverse events attributable to the injection procedure. The most common adverse event was urinary tract infection, reported by 8 patients. Four patients reported de novo urinary urgency; in all cases, this resolved within 3 months.

Eight-year outcomes were reported by Mouritsen et al. (2014) for 24 women, of whom 15 (62.5%) had no further treatment, 1 received a second treatment with hydrogel, and 7 had placement of mid-urethral slings. (16) Subjectively, 44% considered their incontinence to be cured or much improved. Vaginal ultrasonography showed visible hydrogel deposits in all patients.

Polydimethylsiloxane (e.g., Silicone, Macroplastique)
FDA approval of polydimethylsiloxane (Macroplastique) was also partly based on a randomized, noninferiority comparison with collagen in women with SUI. The results of this trial were published by Ghoneim et al. (2009). (17) The trial was single-blind; patients, but not providers, were blinded. At 12 months, Macroplastique was found to be noninferior to collagen in terms of the primary efficacy variable, and improvement in the Stamey Urinary Incontinence Scale. Seventy-five (61%) of 122 patients in the Macroplastique group and 60 (48%) of 125 patients in the collagen group improved at least 1 Stamey grade ($p<.001$ for noninferiority). Twelve of the 247 randomized patients were excluded from the analysis. Two-year data on 67 of the 75 women who responded to treatment with Macroplastique were published Ghoneim et al. (2010). (18) Fifty-six (84%) of the 67 patients had sustained treatment success at 24 months, defined as an improvement of at least 1 Stamey grade over baseline. Forty-five (67%) of the 67 patients evaluated at 24 months were dry (Stamey grade 0). The long-term analysis was limited because it only included a portion of responders from 1 arm of the trial. The analysis included 67 (55%) of 122 patients originally randomized to Macroplastique and did not provide data on the comparison group.

<u>Non-Food and Drug Administration-Approved Bulking Agents</u>
Dextranomer/Hyaluronic Acid (e.g., Zuidex) With an Injection System (e.g., Implacer)
Dextranomer/hyaluronic acid (Zuidex®; AstraZeneca) with an injection system (Implacer®; Q-Med AB) is used to deliver the bulking agent in the outpatient clinic setting without endoscopy. An industry-sponsored (Q-Med) randomized noninferiority trial conducted in North America compared the Zuidex system plus the Implacer with Contigen. As reported by Lightner et al. (2009), patients were blinded to treatment group. (19) The primary study outcome was the proportion of women who had a 50% or greater reduction in urinary leakage on provocation testing from baseline to 12 months after the final treatment (up to 3 treatments were permitted). The primary outcome was achieved by 65% of Zuidex-treated women compared with 84% in the Contigen group; noninferiority of Zuidex was not established. The trial was limited by a high rate of missing data; primary outcomes data were missing for 35% of randomized patients.

An open multicenter study from Europe by Chapple et al. (2005) reported on a 12-month 77% positive response rate (reduction ≥50% for provocation test urinary leakage) with the dextranomer/hyaluronic acid (Zuidex system with Implacer) in 142 women who met strict inclusion and exclusion criteria. (20) Similar to the North American trial, this study had a high dropout rate (24%), an unrepresentative patient population, and lacked a comparison group. Twenty-one women in this study were followed for a mean of 6.7 years after treatment with the Zuidex system. (21) At this long-term follow-up, 7 (33%) of 21 were continent, but 6 of the 7 had had other continence procedures since their Zuidex injections.

Polytetrafluoroethylene (e.g., Teflon)
No published clinical trials were identified on polytetrafluoroethylene as a bulking agent.

Bulking Agents Not Requiring Food and Drug Administration Approval
Autologous Fat and Autologous Ear Chondrocytes
Other materials have been used as bulking agents but have not demonstrated the same sustained effectiveness as cross-linked collagen or carbon-coated beads. In a double-blind RCT of 56 women that compared periurethral injections of autologous fat (treatment group) with saline (placebo group), Lee et al. (2001) found that periurethral fat injections were not more efficacious than placebo for treating stress incontinence. (22) At 3 months, only 6 (22.2%) of 27 patients in the treatment group and 6 (20.7%) of 29 in the placebo group were cured or improved. In addition, 1 death occurred as a result of a pulmonary fat embolism. In another clinical trial of 32 women, Bent et al. (2001) reported that 50% of patients remained dry for 12 months after receiving a single outpatient injection of harvested autologous auricular cartilage. (23) While autologous substances have a nonimmunogenic advantage, their use may be limited by resorption and fibrous replacement along with local discomfort associated with harvesting procedures.

Autologous Cellular Therapy
Strasser et al. (2007) published the first RCT using autologous cell therapy to treat SUI. (24) While widely cited as an important advance in the field, the *Lancet* retracted publication of this trial in 2008 due to ethical and quality concerns. (25)

Pooled safety data from 80 patients in 2 phase 1/2 dose-response trials from Cook MyoSite were reported by Peters et al. (2014). (26) Additionally, in 2018, Jankowski et al. (2018) conducted a randomized, double-blind, placebo-controlled, multicenter trial of intra-sphincteric autologous muscle-derived cells that aimed to enroll 150 female subjects with predominant SUI. (27) Results of an interim analysis revealed an unexpectedly high placebo response rate (90%) using the composite primary outcome, which prevented assessment of the treatment effect as designed and thus enrollment was halted at 61% of planned subjects.

Kaufman et al. (2024) conducted a double-blind RCT using autologous cell therapy to treat SUI. (28) Adult women (N=297) were randomized 2:1 to either autologous cell therapy or placebo, respectively, and stratified by severity of incontinence and prior SUI surgery. After 12 months, patients receiving placebo could opt to receive open-label autologous cell therapy. At 12

months, the proportion of patients achieving the primary endpoint of ≥50% SUI episode reduction was not statistically significant between treatment groups (52% vs 53.6%; p=.798). Adverse events related to treatment were reported in 9.5% of patients receiving autologous cell therapy compared to 6.1% of patients receiving placebo.

Section Summary: Urinary Incontinence

A number of RCTs and a Cochrane review of RCTs evaluating periurethral bulking agents for the treatment of urinary incontinence have been published. The trials vary by bulking agents used and comparator interventions (e.g., placebo, conservative therapy, surgical procedure, another bulking agent). Due to this heterogeneity across studies, and the small number of studies in each category, Cochrane reviewers were unable to draw specific conclusions about the efficacy of specific bulking agents compared with alternative treatments. Additionally, authors of another recent systematic review concluded that bulking agents were less effective than surgical procedures regarding subjective improvement after treatment, with no difference between the interventions with regard to complications. Cross-linked collagen is the most well-established bulking agent, but it was withdrawn from the market. Results from available trials have suggested that carbon-coated spheres, calcium hydroxylapatite, polyacrylamide hydrogel, and polydimethylsiloxane have efficacy for treating incontinence that is similar to cross-linked collagen. For other agents (e.g., autologous cellular therapy, autologous fat, autologous ear chondrocytes, Teflon), there are few RCTs and little evidence of efficacy.

Fecal Incontinence

Clinical Context and Therapy Purpose

The purpose of injectable bulking agents in individuals who have fecal incontinence is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this policy.

Populations

The relevant population of interest is individuals with fecal incontinence.

Interventions

The therapy being considered is injectable bulking agents.

Comparators

The following therapies are currently being used to make decisions about fecal incontinence: conservative therapy, sacral nerve stimulation, and surgery.

Outcomes

The general outcomes of interest are symptom reduction, symptom recurrence, and treatment-related adverse events. Bulking agents may or may not be curative, and follow-up injection may be necessary within 6 months. Beneficial effects may last between 3 and 12 months.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies;
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought;
- Studies with duplicative or overlapping populations were excluded.

Systematic Reviews

A comparative effectiveness review, conducted by Forte et al. (2016) for the Agency for Healthcare Research and Quality, which has since been archived, evaluated treatments for fecal incontinence. (29) Reviewers found low strength of evidence from 2 RCTs that dextranomer anal bulking injections (NASHA Dx, Solesta) were more effective than sham injections on some outcome measures (i.e., 50% reduction in episodes, number of incontinence-free days, quality of life) but not more effective than sham on fecal incontinence severity or frequency, and no more effective than pelvic floor muscle training with biofeedback on fecal incontinence severity or quality of life. There was moderate strength of evidence from 2 RCTs comparing Durasphere with a non-FDA approved bulking agent that off-label use of Durasphere reduced fecal incontinence severity for up to 6 months, with diminishing improvements after that time.

Maeda et al. (2013) updated a Cochrane review assessing perianal injectable bulking agents for treating fecal incontinence. (30) Reviewers identified 5 RCTs (N=382) comparing bulking agents with placebo, no intervention, or an alternative intervention. The 5 trials all included adults with internal anal sphincter dysfunction or passive fecal incontinence who had failed previous conservative treatments (e.g., pelvic floor muscle training). One of the 5 trials (detailed next) used the FDA-approved bulking agent dextranomer in stabilized hyaluronic acid (Solesta). Two trials used a placebo or sham control, 2 compared different bulking agents, and the fifth trial compared 2 methods of injecting the same agent. The length of follow-up ranged from 3 to 12 months. Four trials were judged to be of high or uncertain risk of bias. The greatest potential source of bias was the lack of (or unclear) blinding of outcome assessment and the lack of blinding of surgeons performing the procedure. Due to heterogeneity among trials, study findings were not pooled. Overall, conclusions on efficacy were limited by the small number of RCTs identified, most of which had methodologic limitations, and lack of long-term follow-up.

Randomized Controlled Trials

The RCT evaluating Solesta, included in the Cochrane review, was an industry-sponsored multicenter trial, reported by Graf et al. (2011), that compared Solesta with sham treatment in 206 adults. (31) To be eligible for inclusion, patients had to have a Cleveland Clinic Florida Fecal Incontinence Score (CCFIS) of 10 or higher, at least 4 documented incontinence episodes in 2 weeks, symptoms for at least 12 months, and failure of at least 1 medically supervised conservative treatment (which could include dietary modification, fiber supplements, or loperamide hydrochloride). Patients received an initial injection, and those with persistent symptoms and no substantial adverse effects at 1 month were offered a second injection. A

total of 112 (86%) patients in the active treatment group and 61 (87%) patients in the sham group received a second procedure. Response to treatment was defined as a reduction in the number of incontinence episodes by 50% or more compared with baseline. The trial was double-blind for the first 6 months of follow-up; at 6 months, patients in the sham group were offered active treatment. Thus, the primary efficacy outcome was assessed at 6 months.

A total of 197 (96%) of 206 randomized patients completed 6-month follow-up and were included in the primary efficacy analysis. Seventy-one (52%) in the active treatment group and 22 (31%) in the sham group had a 50% or greater reduction in incontinence episodes at 6 months. The difference between groups was statistically significant (odds ratio: 2.36; 95% CI, 1.24 to 4.47; p=.009). Findings for secondary outcomes at 6 months were mixed. For example, the mean increase in the number of incontinence-free days was significantly higher in the active treatment group (3.1) than the sham group (1.7; p=.016), but the median decrease in the number of incontinence episodes did not differ significantly between groups (6.0 vs 3.0, respectively; p=.09). Moreover, change in the CCFIS did not differ significantly between groups at 6 months (2.5 points for active treatment vs 1.7 points for sham treatment). Quality of life was measured by the Fecal Incontinence Quality of Life instrument, which has 4 subscales. One of the 4 subscales (coping and behavior) improved significantly more in the treatment group than in the sham group at 6 months. Change in scores on the other 3 subscales (lifestyle, depression and self-perception, embarrassment) did not differ significantly between groups at 6 months. Trialists did not report the proportion of patients continent at follow-up, either as a primary or secondary outcome.

During the 6-month blinded treatment phase, 128 adverse events were reported in the active treatment group and 29 in the sham group. The most common adverse event in the active treatment group was proctalgia, which occurred in 19 (14%) patients (vs 2 [3%] patients in the sham group). Moreover, 10 (7%) patients in the active treatment group and 1 (1%) patient in the sham group had a rectal hemorrhage. Injection site bleeding occurred in 12 (17%) patients in the sham group and in 7 (5%) patients in the active treatment group. Two serious adverse events were reported, both in the active treatment group (1 rectal abscess, 1 prostate abscess).

Mellgren et al. (2014) published long-term follow up from the 136 patients originally treated with active treatment in the 6-month trial and found sustained response at both 12 months (57.4%) and 36 months (52.2%). (32) Mean CCFIS decreased from 14.3 at baseline to 10.5 at month 36. Overall incontinence-free days increased from 4.4 at baseline to 8.1 at 36 months. A total of 20 additional treatment-related adverse events after the 6-month randomized phase were documented. The most frequent events were injection site nodule (n=3) and proctalgia (n=3).

Dehli et al. (2013) published findings of an RCT evaluating Solesta. (33) A total of 126 adults with fecal incontinence were randomized to injectable bulking agents (n=62) or a 6-month biofeedback intervention (n=64). Patients in the bulking agent group who reported minor or no symptom improvement at 3 months received a second injection. The primary efficacy outcome was incontinence severity, as measured by the St. Mark's Fecal Incontinence Grading System

score, which ranges from 0 (perfect continence) to 24 (maximal incontinence). A St. Mark's score of at least 4 was required for study participation. Ten (8%) patients dropped out of the study before 6 months. At the 6-month follow-up, the mean St. Mark's score in the biofeedback group had decreased from 12.6 points (95% CI, 11.4 to 13.8) at baseline to 9.2 points (95% CI, 7.9 to 10.5). In the bulking agents group, mean scores were 12.9 (95% CI, 11.8 to 14.0) at baseline and 8.9 (95% CI, 7.6 to 10.2) at 6 months. This difference between groups in St. Mark's score reduction was not statistically significant. In addition, change in St. Mark's score did not differ between groups at 24 months, and only 61 (49%) patients completed the 24-month follow-up. Three of the first 10 patients in the bulking agent group developed infections at the injection site and underwent treatment; subsequent patients in this group received prophylactic antibiotics.

Uncontrolled Trials

Longer term data on Solesta are available from an uncontrolled study conducted by La Torre et al. (2013). (34) A total of 115 patients in Europe and Canada with fecal incontinence received 1 Solesta treatment and an optional retreatment after 1 month. Eighty-three (72%) of 115 patients completed the 24-month follow-up. The primary efficacy end point was a response to treatment, defined as a minimum 50% reduction from baseline in the number of fecal incontinence episodes recorded in a 28-day diary. At the 24-month follow-up, 52 (63%) of 83 patients with data available had responded to treatment. The median number of incontinence-free days in a 28-day period increased from 14.6 at baseline to 21.7 at 24 months. The study lacked a comparison group and had a high dropout rate.

Quiroz et al. (2023) published an open-label, single-arm, FDA-mandated, long-term study evaluating the long-term efficacy and safety of Solesta in patients (N=283) who had failed conservative therapy. (35) The study was conducted at 18 sites in the U.S., and patients received 1 dose of Solesta within 3 months of baseline and a repeat dose at approximately 3 months after the first dose if necessary. The primary endpoint evaluated the need for fecal incontinence reintervention at 36 months. The enrolled patients were largely White (91.8%) and female (85.5%). The majority of patients (76.7%) received 2 treatments. At 36 months the need for reinterventions was 20.8% (95% CI, 15.1 to 26.6). CCFIS scores decreased from 13.5 at baseline to 9.2 at the final visit ($p<.0001$). There were no serious device-related adverse events or death, but 15.2% of patients reported 92 nonserious device-related adverse events with gastrointestinal-related events the most commonly reported. Limitations of this study include a high dropout rate (32%), limited demographic variability, and lack of a comparison group.

Section Summary: Fecal Incontinence

Several RCTs and systematic reviews of RCTs on bulking agents for the treatment of fecal incontinence have been published. A 2016 comparative effectiveness review from the Agency for Healthcare Research and Quality evaluated 2 RCTs with the FDA-approved product NASHA Dx (Solesta) and 2 RCTs with Durasphere. One RCT using NASHA Dx found that, compared with sham, NASHA Dx improved some outcomes but not others. The other RCT did not find a significant difference in efficacy between NASHA Dx and biofeedback. Two other RCTs evaluating Durasphere (off-label in the U.S.) found short-term improvements in fecal

incontinence severity. Overall, the evidence is not sufficient to conclude that bulking agents are an effective treatment for fecal incontinence. Corroboration of the single positive comparative trial is needed, and controlled trials with longer follow-up are important to determine the durability of any treatment effect.

Summary of Evidence

For individuals who have stress urinary incontinence (SUI) who receive injectable bulking agents, the evidence includes randomized controlled trials (RCTs) and systematic reviews of RCTs. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. The trials vary by bulking agents used and comparator interventions (e.g., placebo, conservative therapy, surgical procedure, another bulking agent). Due to this heterogeneity across studies, and the small number of studies in each category, Cochrane reviewers were unable to draw specific conclusions about the efficacy of specific bulking agents compared with alternative treatments. Additionally, authors of another recent systematic review concluded that bulking agents were less effective than surgical procedures regarding subjective improvement after treatment, with no difference between the interventions with regard to complications. Studies have shown that cross-linked collagen improves the net health outcome (i.e., it is effective in some patients who have failed conservative treatment with fewer adverse events than surgery), although products that cross-link in such a way are no longer commercially available. There is evidence that the U.S. Food and Drug Administration (FDA) approved carbon-coated spheres, calcium hydroxylapatite, polyacrylamide hydrogel and polydimethylsiloxane have efficacy for treating incontinence, and further that they produce outcomes with a safety profile similar to cross-linked collagen. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have fecal incontinence who receive injectable bulking agents, the evidence includes RCTs and systematic reviews of RCTs. Relevant outcomes are symptoms, functional outcomes, quality of life, and treatment-related morbidity. A comparative effectiveness review from the Agency for Healthcare Research and Quality evaluated 2 RCTs with the FDA approved product NASHA Dx (Solesta) and 2 RCTs with Durasphere (off-label in the United States). One RCT comparing NASHA Dx with sham found that NASHA Dx improved some outcomes but not others. The other RCT did not find a significant difference in efficacy between NASHA Dx and biofeedback. Two additional RCTs evaluating Durasphere found only short-term improvements in fecal incontinence severity. Controlled trials with longer follow-up are needed to determine the durability of any treatment effect. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Practice Guidelines and Position Statements

Urinary Incontinence

American College of Obstetricians and Gynecologists

In 2015 (reaffirmed in 2025), the American College of Obstetricians and Gynecologists (ACOG) updated its practice bulletin on urinary incontinence in women. (36) The practice bulletin stated that "urethral bulking injections are a relatively noninvasive treatment for stress urinary incontinence that may be appropriate if surgery has failed to achieve adequate symptom

reduction, if symptoms recur after surgery, in women with symptoms who do not have urethral mobility, or in older women with comorbidities who cannot tolerate anesthesia or more invasive surgery. However, urethral bulking agents are less effective than surgical procedures such as sling placement and are rarely used as primary treatment for stress urinary incontinence." There was insufficient evidence to recommend any specific bulking agent.

American Urogynecologic Society
In 2024, the American Urogynecologic Society published a clinical practice statement on urethral bulking. (37) They recommended that urethral bulking agents are indicated in cases of stress urinary incontinence (SUI), and that intrinsic sphincter deficiency is not predictive of patient outcomes (Grade B evidence; strength of recommendation [SOR]: strong recommendation). They also stated that urethral bulking agents may be considered for initial management of SUI, however the grade of evidence and strength of the recommendation were weaker (Grade C evidence; SOR: recommendation).

American Urological Association and Society of Urodynamics
The 2017 joint guidelines on the surgical treatment of female SUI from the American Urological Association and Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction stated that bulking agents are an option for patients considering surgery for SUI. (38) The guidelines also stated that there are few long-term data on the efficacy of bulking agents and that retreatment is common. These recommendations are consistent in the 2023 update to the guidelines. (39)

National Institute for Health and Care Excellence (NICE)
In 2019, NICE updated its guidance on urinary incontinence in women. (40) The updated guidance recommends "intramural bulking agents to manage stress urinary incontinence if alternative surgical procedures are not suitable for or acceptable to the woman." The patient should be educated that these are permanent injectable materials, repeat injections may be needed, and there is limited evidence on long-term effectiveness and adverse events.

Fecal Incontinence
American College of Obstetricians and Gynecologists
In 2019 (reaffirmed 2023), ACOG published a practice bulletin on the clinical management of fecal incontinence in women. (41) The College stated that "anal sphincter bulking agents may be effective in decreasing fecal incontinence episodes up to 6 months and can be considered as a short-term treatment option for fecal incontinence in women who have failed more conservative treatments." This recommendation is based on limited or inconsistent scientific evidence.

American Gastroenterological Association
In 2017, the American Gastroenterological Association (AGA) published guidance on surgical interventions and the use of device-aided therapy for the treatment of fecal incontinence and defecatory disorders. (42) The AGA recommends, "Perianal bulking agents such as intra-anal

injection of dextranomer may be considered when conservative measures and biofeedback therapy fail."

American Society of Colon and Rectal Surgeons
In 2023, the American Society of Colon and Rectal Surgeons updated its practice parameters for the treatment of fecal incontinence. (43) The Society states, "Injection of biocompatible bulking agents into the anal canal is not routinely recommended for the treatment of FI [fecal incontinence]" based on low quality evidence showing limited improvement over placebo, diminishing long-term results, and cost.

National Institute for Health and Care Excellence
In 2007, NICE published guidance on injectable bulking agents for treating fecal incontinence. (44) The guidance stated that there is insufficient evidence to support the safety and efficacy of injectable bulking agents for fecal incontinence.

Medicare National Coverage
The 1996 Medicare National Coverage Determination for Incontinence Control Devices (230.10) addressed collagen implants but not other types of bulking agents. (45) Specific coverage information on collagen implants is as follows:

"Coverage of a collagen implant, and the procedure to inject it, is limited to the following types of patients with stress urinary incontinence due to ISD [intrinsic sphincteric deficiency]:

- Male or female patients with congenital sphincter weakness secondary to conditions such as myelomeningocele or epispadias;
- Male or female patients with acquired sphincter weakness secondary to spinal cord lesions;
- Male patients following trauma, including prostatectomy and/or radiation; and
- Female patients without urethral hypermobility and with abdominal leak point pressures of 100 cm H_2O or less.

Patients whose incontinence does not improve with 5 injection procedures (5 separate treatment sessions) are considered treatment failures, and no further treatment of urinary incontinence by collagen implant is covered. Patients who have a recurrence of incontinence following successful treatment with collagen implants in the past (e.g., 6 to 12 months previously) may benefit from additional treatment sessions. Coverage of additional sessions may be allowed but must be supported by medical justification."

No national coverage determination was identified on injectable bulking agents for treating fecal incontinence.

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this policy are listed in Table 1.

Table 1. Summary of Key Trials

NCT Number	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT03474653	Latitude-An Observational Study of Patient Choice and the Urethral Bulking Agent, Bulkamid, Used for the First Line Treatment for Stress Urinary Incontinence and the Impact on a Subsequent Mid Urethral Sling	399	Jun 2024
NCT03811821	Comparative Effectiveness of Biofeedback, Sacral Nerve Stimulation, and Injectable Bulking Agents for Treatment of Fecal Incontinence: The Fecal Incontinence Treatment (FIT) Study	275	Dec 2025
NCT06480227	A Randomized Trial of Transurethral Bulking Agent Injection Versus Single-Incision Sling for Stress Urinary Incontinence	358	Aug 2029

NCT: national clinical trial.

Coding

Procedure codes on Medical Policy documents are included **only** as a general reference tool for each policy. **They may not be all-inclusive.**

The presence or absence of procedure, service, supply, or device codes in a Medical Policy document has no relevance for determination of benefit coverage for members or reimbursement for providers. **Only the written coverage position in a Medical Policy should be used for such determinations.**

Benefit coverage determinations based on written Medical Policy coverage positions must include review of the member's benefit contract or Summary Plan Description (SPD) for defined coverage vs. non-coverage, benefit exclusions, and benefit limitations such as dollar or duration caps.

CPT Codes	51715, 0963T
HCPCS Codes	L8603, L8604, L8605, L8606

*Current Procedural Terminology (CPT®) ©2024 American Medical Association: Chicago, IL.

References

1. Gorina Y, Schappert S, Bercovitz A, et al. Prevalence of incontinence among older Americans. Vital Health Stat 3. Jun 2014; (36):1-33. PMID 24964267
2. Agency for Health Care Policy and Research. Clinical Practice Guideline. Urinary Incontinence in Adults. Rockville, MD: Department of Health and Human Services; 1996.
3. Corcos J, Collet JP, Shapiro S, et al. Multicenter randomized clinical trial comparing surgery and collagen injections for treatment of female stress urinary incontinence. Urology. May 2005; 65(5):898-904. PMID 15882720

4. Hoe V, Haller B, Yao HH, et al. Urethral bulking agents for the treatment of stress urinary incontinence in women: A systematic review. Neurourol Urodyn. Aug 2021; 40(6):1349-1388. PMID 34015151
5. Pivazyan L, Kasyan G, Grigoryan B, et al. Effectiveness and safety of bulking agents versus surgical methods in women with stress urinary incontinence: a systematic review and meta-analysis. Int Urogynecol J. Apr 2022; 33(4):777-787. PMID 34351463
6. Kirchin V, Page T, Keegan PE, et al. Urethral injection therapy for urinary incontinence in women. Cochrane Database Syst Rev. Jul 25 2017; 7(7):CD003881. PMID 28738443
7. Kirchin V, Page T, Keegan PE, et al. Urethral injection therapy for urinary incontinence in women. Cochrane Database Syst Rev. Feb 15 2012; (2):CD003881. PMID 22336797
8. Davila GW. Nonsurgical outpatient therapies for the management of female stress urinary incontinence: long-term effectiveness and durability. Adv Urol. 2011; 2011:176498. PMID 21738529
9. Lightner D, Calvosa C, Andersen R, et al. A new injectable bulking agent for treatment of stress urinary incontinence: results of a multicenter, randomized, controlled, double-blind study of Durasphere. Urology. Jul 2001; 58(1):12-15. PMID 11445471
10. Mayer RD, Dmochowski RR, Appell RA, et al. Multicenter prospective randomized 52-week trial of calcium hydroxylapatite versus bovine dermal collagen for treatment of stress urinary incontinence. Urology. May 2007; 69(5):876-880. PMID 17482925
11. Sokol ER, Karram MM, Dmochowski R. Efficacy and safety of polyacrylamide hydrogel for the treatment of female stress incontinence: a randomized, prospective, multicenter North American study. J Urol. Sep 2014; 192(3):843-849. PMID 24704117
12. Itkonen Freitas AM, Mentula M, Rahkola-Soisalo P, et al. Tension-Free Vaginal Tape Surgery versus Polyacrylamide Hydrogel Injection for Primary Stress Urinary Incontinence: A Randomized Clinical Trial. J Urol. Feb 2020; 203(2):372-378. PMID 31479396
13. Pai A, Al-Singary W. Durability, safety and efficacy of polyacrylamide hydrogel (Bulkamid®) in the management of stress and mixed urinary incontinence: three year follow up outcomes. Cent European J Urol. 2015; 68(4):428-433. PMID 26855795
14. Lose G, Sørensen HC, Axelsen SM, et al. An open multicenter study of polyacrylamide hydrogel (Bulkamid®) for female stress and mixed urinary incontinence. Int Urogynecol J. Dec 2010; 21(12):1471-1477. PMID 20645077
15. Leone Roberti Maggiore U, Alessandri F, Medica M, et al. Outpatient periurethral injections of polyacrylamide hydrogel for the treatment of female stress urinary incontinence: effectiveness and safety. Arch Gynecol Obstet. Jul 2013; 288(1):131-137. PMID 23371485
16. Mouritsen L, Lose G, Møller-Bek K. Long-term follow-up after urethral injection with polyacrylamide hydrogel for female stress incontinence. Acta Obstet Gynecol Scand. Feb 2014; 93(2):209-212. PMID 24372312
17. Ghoniem G, Corcos J, Comiter C, et al. Cross-linked polydimethylsiloxane injection for female stress urinary incontinence: results of a multicenter, randomized, controlled, single-blind study. J Urol. Jan 2009; 181(1):204-210. PMID 19013613
18. Ghoniem G, Corcos J, Comiter C, et al. Durability of urethral bulking agent injection for female stress urinary incontinence: 2-year multicenter study results. J Urol. Apr 2010; 183(4):1444-1449. PMID 20171691

19. Lightner D, Rovner E, Corcos J, et al. Randomized controlled multisite trial of injected bulking agents for women with intrinsic sphincter deficiency: mid-urethral injection of Zuidex via the Implacer versus proximal urethral injection of Contigen cystoscopically. Urology. Oct 2009; 74(4):771-775. PMID 19660800
20. Chapple CR, Haab F, Cervigni M, et al. An open, multicentre study of NASHA/Dx Gel (Zuidex) for the treatment of stress urinary incontinence. Eur Urol. Sep 2005; 48(3):488-494. PMID 15967568
21. Lone F, Sultan AH, Thakar R. Long-term outcome of transurethral injection of hyaluronic acid/dextranomer (NASHA/Dx gel) for the treatment of stress urinary incontinence (SUI). Int Urogynecol J. Nov 2010; 21(11):1359-1364. PMID 20571764
22. Lee PE, Kung RC, Drutz HP. Periurethral autologous fat injection as treatment for female stress urinary incontinence: a randomized double-blind controlled trial. J Urol. Jan 2001; 165(1):153-158. PMID 11125386
23. Bent AE, Tutrone RT, McLennan MT, et al. Treatment of intrinsic sphincter deficiency using autologous ear chondrocytes as a bulking agent. Neurourol Urodyn. 2001; 20(2):157-165. PMID 11170190
24. Strasser H, Marksteiner R, Margreiter E, et al. Autologous myoblasts and fibroblasts versus collagen for treatment of stress urinary incontinence in women: a randomised controlled trial. Lancet. Jun 30 2007; 369(9580):2179-2186. PMID 17604800
25. Kleinert S, Horton R. Retraction--autologous myoblasts and fibroblasts versus collagen [corrected] for treatment of stress urinary incontinence in women: a [corrected] randomised controlled trial. Lancet. Sep 06 2008; 372(9641):789-790. PMID 18774408
26. Peters KM, Dmochowski RR, Carr LK, et al. Autologous muscle derived cells for treatment of stress urinary incontinence in women. J Urol. Aug 2014; 192(2):469-476. PMID 24582537
27. Jankowski RJ, Tu LM, Carlson C, et al. A double-blind, randomized, placebo-controlled clinical trial evaluating the safety and efficacy of autologous muscle derived cells in female subjects with stress urinary incontinence. Int Urol Nephrol. Dec 2018; 50(12):2153-2165. PMID 30324580
28. Kaufman MR, Goldman HB, Chermansky CJ, et al. Iltamiocel Autologous Cell Therapy for the Treatment of Female Stress Urinary Incontinence: A Double-Blind, Randomized, Stratified, Placebo-Controlled Trial. Neurourol Urodyn. Nov 2024; 43(8):2290-2299. PMID 39282854
29. Forte ML, Andrade KE, Butler M, et al. Treatments for Fecal Incontinence (Comparative Effectiveness Review No. 165). Rockville, MD: Agency for Healthcare Research and Quality; 2016.
30. Maeda Y, Laurberg S, Norton C. Perianal injectable bulking agents as treatment for faecal incontinence in adults. Cochrane Database Syst Rev. Feb 28 2013; 2013(2):CD007959. PMID 23450581
31. Graf W, Mellgren A, Matzel KE, et al. Efficacy of dextranomer in stabilised hyaluronic acid for treatment of faecal incontinence: a randomised, sham-controlled trial. Lancet. Mar 19 2011; 377(9770):997-1003. PMID 21420555
32. Mellgren A, Matzel KE, Pollack J, et al. Long-term efficacy of NASHA Dx injection therapy for treatment of fecal incontinence. Neurogastroenterol Motil. Aug 2014; 26(8):1087-1094. PMID 24837493

33. Dehli T, Stordahl A, Vatten LJ, et al. Sphincter training or anal injections of dextranomer for treatment of anal incontinence: a randomized trial. Scand J Gastroenterol. Mar 2013; 48(3):302-310. PMID 23298304
34. La Torre F, de la Portilla F. Long-term efficacy of dextranomer in stabilized hyaluronic acid (NASHA/Dx) for treatment of fecal incontinence. Colorectal Dis. May 2013; 15(5):569-574. PMID 23374680
35. Quiroz LH, Galliano DE, da Silva G, et al. Efficacy and Safety of a Nonanimal Stabilized Hyaluronic Acid/Dextranomer in Improving Fecal Incontinence: A Prospective, Single-Arm, Multicenter, Clinical Study With 36-Month Follow-up. Dis Colon Rectum. Feb 01 2023; 66(2):278-287. PMID 35001051
36. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin No. 155: Urinary Incontinence in Women. Obstet Gynecol. 2015; 126(5):e66-e81. PMID 26488524
37. Fleischmann N, Chughtai B, Plair A, et al. Urethral Bulking. Urogynecology (Phila). Aug 01 2024; 30(8):667-682. PMID 39051928
38. Kobashi KC, Albo ME, Dmochowski RR, et al. Surgical Treatment of Female Stress Urinary Incontinence: AUA/SUFU Guideline. J Urol. Oct 2017; 198(4):875-883. PMID 28625508
39. Kobashi KC, Vasavada S, Bloschichak A, et al. Updates to Surgical Treatment of Female Stress Urinary Incontinence (SUI): AUA/SUFU Guideline (2023). J Urol. Jun 2023; 209(6):1091-1098. PMID 37096580
40. National Institute for Health and Care Excellence (NICE). Urinary incontinence and pelvic organ prolapse in women: management [NG123] (2019). Available at: <https://www.nice.org.uk> (accessed September 8, 2025).
41. ACOG Practice Bulletin No. 210: Fecal Incontinence. Obstet Gynecol. Apr 2019; 133(4):e260-e273. PMID 30913197
42. Bharucha AE, Rao SSC, Shin AS. Surgical Interventions and the Use of Device-Aided Therapy for the Treatment of Fecal Incontinence and Defecatory Disorders. Clin Gastroenterol Hepatol. Dec 2017; 15(12):1844-1854. PMID 28838787
43. Bordeianou LG, Thorsen AJ, Keller DS, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Fecal Incontinence. Dis Colon Rectum. May 2023; 66(5):647-661. PMID 40324433
44. National Institute for Health and Care Excellence (NICE). Injectable bulking agents for fecal incontinence [IPG210] (2007). Available at: <https://www.nice.org.uk> (accessed September 9, 2025).
45. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Incontinence Control Devices (230.10). 1996; Available at: <https://www.cms.gov> (accessed September 9, 2025).

Centers for Medicare and Medicaid Services (CMS)

The information contained in this section is for informational purposes only. HCSC makes no representation as to the accuracy of this information. It is not to be used for claims adjudication for HCSC Plans.

The Centers for Medicare and Medicaid Services (CMS) does have a national Medicare coverage position. Coverage may be subject to local carrier discretion.

A national coverage position for Medicare may have been changed since this medical policy document was written. See Medicare's National Coverage at <https://www.cms.hhs.gov>.

Policy History/Revision	
Date	**Description of Change**
12/15/2025	Document updated. The following changes were made to Coverage: 1) Modified both medically necessary and experimental, investigational and/or unproven statements related to treatment of stress urinary incontinence without change to intent; and 2) Moved content from NOTE 1 to Policy Guidelines. Added reference 28.
01/01/2025	Document updated with literature review. Coverage unchanged. Added reference 36.
01/01/2024	Document updated with literature review. Coverage unchanged. References 27, 31, 34, 37, 40-41, and 43 added; others removed.
05/15/2022	Document updated with literature review. Coverage unchanged. References 4-6, 12 and 38 added.
05/01/2021	Document updated with literature review. Coverage changed to include Polyacrylamide hydrogel as conditionally medically necessary. FDA approved Bulkamid® Urethral Bulking System added to the Regulatory Status section. Reference 12 added.
10/15/2020	Reviewed. No changes.
11/15/2019	Document updated with literature review. Coverage unchanged. The following references were added/updated: 1, 36 and 40.
10/15/2018	Reviewed. No changes.
12/15/2017	Document updated with literature review. Coverage statement changed to note that the listed periurethral bulking agents may be considered medically necessary for the treatment of stress urinary incontinence (SUI), when there is no improvement in incontinence for at least three months (replacing the previously noted 12 months) during which time, conservative therapy(s) have been attempted and failed. In addition, a note has been added to define conservative therapy(s).
11/01/2016	Reviewed. No changes.
08/01/2015	Document updated with literature review. Coverage revised to remove reference to cross-linked collagen (e.g., Contigen®) as a medically necessary periurethral bulking agent. Contigen production was discontinued in 2011. Added cross-linked collagen to experimental, investigational and/or unproven listing as this product is no longer produced.
05/01/2014	Document updated with literature review. The following was added to the coverage. The use of perianal bulking agents to treat fecal incontinence is considered experimental, investigational and/or unproven. CPT/HCPCS

	code(s) updated. Document title changed from Periurethral Bulking Agents for the Treatment of Urinary Incontinence.
01/15/2013	Document updated with literature review. The following was added to the coverage. The use of periurethral bulking agents to treat urge urinary incontinence is considered experimental, investigational and unproven.
05/15/2009	Coverage revised
07/15/2008	Revised/updated entire document. This policy is no longer scheduled for routine literature review and update.
05/01/2007	Revised/updated entire document
10/01/2003	Revised/updated entire document
06/01/2001	CPT/HCPCS code(s) updated
09/01/1999	New medical document