BlueCross BlueShield Federal Employee Program.

FEP Medical Policy Manual

FEP 7.01.19 Injectable Bulking Agents for the Treatment of Urinary and Fecal Incontinence

Effective Policy Date: January 1, 2022

Original Policy Date: December 2012

Related Policies:

1.01.17 - Pelvic Floor Stimulation as a Treatment of Urinary and Fecal Incontinence
7.01.102 - Periureteral Bulking Agents as a Treatment of Vesicoureteral Reflux
7.01.106 - Percutaneous Tibial Nerve Stimulation

Injectable Bulking Agents for the Treatment of Urinary and Fecal Incontinence

Description

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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 1 for treating fecal incontinence.

OBJECTIVE

The objective of this evidence review is to determine whether injectable bulking agents improve the net health outcome for individuals with stress urinary incontinence or fecal incontinence.

POLICY STATEMENT

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.

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

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

The use of periurethral bulking agents to treat urge urinary incontinence is considered **investigational**.

The use of perianal bulking agents to treat fecal incontinence is considered **not medically necessary**.

POLICY GUIDELINES

Patients 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 patients amenable to these treatments.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

Periurethral bulking agents may benefit both men and women with stress urinary incontinence. However, only Contigen, which is no longer commercially available, has FDA approval for use in men and women.

FDA 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 (Merz Aesthetics, previously BioForm Medical), spherical particles of calcium hydroxylapatite, suspended in a gel carrier, was approved.
- In 2006, Macroplastique (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), 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

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 (eg, 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 (ie, 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 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.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

Urinary Incontinence

American Urological Association and Society of Urodynamics

The 2017 joint guidelines on the surgical treatment of female stress urinary incontinence (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.[35.] The guidelines also stated that there are few long-term data on the efficacy of bulking agents and that retreatment is common.

National Institute for Health and Care Excellence

In 2015, the National Institute for Health and Care Excellence updated its guidance on urinary incontinence in women.[36.] The updated guidance recommended considering "intramural bulking agents (silicone, carbon-coated zirconium beads or hyaluronic acid/dextran copolymer) for the management of stress UI [urinary incontinence] if conservative management has failed. Women should be made aware that:

- repeat injections may be needed to achieve efficacy

- efficacy diminishes with time
- efficacy is inferior to that of synthetic tapes or autologous rectus fascial slings."

American College of Obstetricians and Gynecologists

In 2016 (reaffirmed in 2019), the American College of Obstetricians and Gynecologists updated its practice bulletin on urinary incontinence in women.[37.] 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.

Fecal Incontinence

American College of Obstetricians and Gynecologists

In 2019, the American College of Obstetricians and Gynecologists published a practice bulletin on the clinical management of fecal incontinence in women.[38.] 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 Society of Colon and Rectal Surgeons

In 2015, the American Society of Colon and Rectal Surgeons updated its practice parameters for the treatment of fecal incontinence.[39.] The Society gave a weak recommendation based on moderate-quality evidence (2B) that injection of bulking agents into the anal canal may help to decrease episodes of passive fecal incontinence. Studies reviewed showed modest short-term improvements, and no study identified showed a long-term benefit of bulking agents.

National Institute for Health and Care Excellence

In 2007, the National Institute for Health and Care Excellence published guidance on injectable bulking agents for treating fecal incontinence.[40.] The guidance stated that there is insufficient evidence to support the safety and efficacy of injectable bulking agents for fecal incontinence.

U.S. Preventive Services Task Force Recommendations

Not applicable.

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.[41.] 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 (eg, 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.

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. Aug 05 2021. 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: 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): 12-5. 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): 876-80. 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): 843-9. 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((R))) in the management of stress and mixed urinary incontinence: three year follow up outcomes. Cent European J Urol. 2015; 68(4): 428-33. PMID 26855795
14. Lose G, Sorensen HC, Axelsen SM, et al. An open multicenter study of polyacrylamide hydrogel (Bulkamid(R)) for female stress and mixed urinary incontinence. Int Urogynecol J. Dec 2010; 21(12): 1471-7. 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): 131-7. PMID 23371485
16. Mouritsen L, Lose G, Moller-Bek K. Long-term follow-up after urethral injection with polyacrylamide hydrogel for female stress incontinence. Acta Obstet Gynecol Scand. Feb 2014; 93(2): 209-12. 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): 204-10. 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): 1444-9. 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): 771-5. 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): 488-94. 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): 1359-64. 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): 153-8. 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): 157-65. 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): 789-90. 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): 469-76. PMID 24582537
27. 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.
28. Maeda Y, Laurberg S, Norton C. Perianal injectable bulking agents as treatment for faecal incontinence in adults. Cochrane Database Syst Rev. Feb 28 2013; (2): CD007959. PMID 23450581
29. Hussain ZI, Lim M, Stojkovic SG. Systematic review of perianal implants in the treatment of faecal incontinence. Br J Surg. Nov 2011; 98(11): 1526-36. PMID 21964680
30. Leung FW. Treatment of fecal incontinence - review of observational studies (OS) and randomized controlled trials (RCT) related to injection of bulking agent into peri-anal tissue. J Interv Gastroenterol. Oct 2011; 1(4): 202-206. PMID 22586538
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. 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): 302-10. PMID 23298304
33. Morris OJ, Smith S, Draganic B. Comparison of bulking agents in the treatment of fecal incontinence: a prospective randomized clinical trial. Tech Coloproctol. Oct 2013; 17(5): 517-23. PMID 23525964
34. La Torre F, de la Portilla F. Long-term efficacy of dextranomer in stabilized hyaluronic acid (NASHA/Dx) for treatment of faecal incontinence. Colorectal Dis. May 2013; 15(5): 569-74. PMID 23374680
35. 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
36. National Institute for Health and Care Excellence (NICE). Urinary incontinence and pelvic organ prolapse in women: management [NG123]. 2019; https://www.nice.org.uk/guidance/ng123. Accessed August 29, 2021.
37. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin No. 155: Urinary Incontinence in Women. Obstet Gynecol. May 2016;127(5):e66-81. PMID 27548423
38. ACOG Practice Bulletin No. 210: Fecal Incontinence. Obstet Gynecol. Apr 2019; 133(4): e260-e273. PMID 30913197
39. Paquette IM, Varma MG, Kaiser AM, et al. The American Society of Colon and Rectal Surgeons' Clinical Practice Guideline for the Treatment of Fecal Incontinence. Dis Colon Rectum. Jul 2015; 58(7): 623-36. PMID 26200676
40. National Institute for Health and Care Excellence (NICE). Injectable bulking agents for faecal incontinence [IPG210]. 2007; https://www.nice.org.uk/guidance/ipg210/chapter/1-guidance. Accessed August 30, 2021.
41. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for Incontinence Control Devices (230.10). 1996; https://www.cms.gov/medicare-coverage-database/details/ncd- details.aspx?NCDId=241&ncdver=1&DocID=230.10&bc=gAAAAAgAAAAAAA%3D%3D&. Accessed August 29, 2021.

POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
December 2012	New policy	
June 2013	Replace policy	Policy expanded to include fecal incontinence. Statement added that perianal bulking agents to treat fecal incontinence is not medically necessary. Title changed to Injectable Bulking Agents for the Treatment of Urinary and Fecal Incontinence. References 19-24, 26 and 27 added; other references renumbered.
June 2014	Replace policy	Policy updated with literature review, adding references 15, 20, 26 and 27. No changes to the policy statement.
September 2015	Replace policy	Policy updated with literature review; references 14, 17, and 22 added; Contigen removed from medically necessary statement as it is no longer available.
March 2017	Replace policy	Policy updated with literature review; references 15 and 24 added; 35-36 updated. Policy statements unchanged.
December 2017	Replace policy	Policy updated with literature review through June 22, 2017; references 32-33 added. Policy statements unchanged.

Date	Action	Description
December 2018	Replace policy	Policy updated with literature review through June 7, 2018; reference 1 added. Policy statements unchanged.
December 2019	Replace policy	Policy updated with literature review through July 11, 2019. Policy statements unchanged.
December 2020	Replace policy	Policy updated with literature review through May 22, 2020; no references added. Policy history for June 2013 corrected to read: Statement added that perianal bulking agents to treat fecal incontinence is NOT medically necessary. Policy statements remain unchanged.
December 2021	Replace policy	Policy updated with literature review through August 29, 2021; references added. Medically necessary policy statement in men and women with stress urinary incontinence who have failed appropriate conservative therapy expanded to include polyacrylamide hydrogel, which is now FDA approved.