POLICY TITLE	**INJECTABLE BULKING AGENTS FOR THE TREATMENT OF URINARY AND FECAL INCONTINENCE**
POLICY NUMBER	**MP- 4.012**

Original Issue Date (Created):	**8/9/2002**
Most Recent Review Date (Revised):	**6/11/2018**
Effective Date:	**8/1/2018**

I. POLICY

The use of carbon-coated spheres (Durasphere®), calcium hydroxylapatite (CaHA) (Coaptite®) or polydimethylsiloxane (Macroplastique®) may be considered **medically necessary** to treat urinary stress incontinence in men and women who have failed conservative therapy.

The use of autologous cellular therapy (e.g., myoblasts, fibroblasts, muscle-derived stem cells, or 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 **investigational.**

There is insufficient evidence to support a conclusion concerning the health outcomes related to their efficacy for the above listed investigational indications.

Policy Guidelines

Patients should have had 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.

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Cross-references

MP-1.033 Sacral Nerve Modulation/Stimulation and Pelvic Floor Stimulation Devices
MP-2.064 Biofeedback and Neurofeedback Therapy
MP-4.034 Transvaginal and Transurethral Radiofrequency Tissue Remodeling for Urinary Stress Incontinence
MP-1.134 Percutaneous Tibial Nerve Stimulation

II. PRODUCT VARIATIONS

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This policy is applicable to all programs and products administered by Capital BlueCross unless otherwise indicated below.

FEP PPO - Refer to FEP Medical Policy Manual MP 7.01.19, Periurethral Bulking Agents for the Treatment of Urinary and Fecal Incontinence. The FEP Medical Policy Manual can be found at: https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies.

III. DESCRIPTION/BACKGROUND

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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 one for treating fecal 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 the tissue bulk and thereby increase resistance to the outflow of urine. The bulking agent is injected into the periurethral tissue as a liquid that then 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 post-prostatectomy incontinence.

Following the success of periurethral bulking agents for treating SUI, bulking agents injected into the anal canal have been proposed for treating fecal incontinence. In particular, bulking agents are a potential treatment for passive fecal incontinence associated with internal anal sphincter (IAS) 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 and pelvic floor muscle exercises, sacral nerve stimulation, and surgical interventions to correct an underlying problem.

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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 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), and ethylene vinyl alcohol copolymer implants (e.g., Tegress, formerly Uryx). Tegress was voluntarily removed from the market due to safety concerns.

Several agents identical to or similar to those used for urinary incontinence e.g., Durasphere, silicone biomaterial, etc. have been studied for the treatment of fecal incontinence. To date, only one bulking agent has been approved by the FDA for treating fecal incontinence. This is a formulation of non-animal stabilized hyaluronic acid/dextranomer in stabilized hyaluronic acid (NASHA Dx) and is marketed by Q-Med 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

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 has not received 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 is hoped that transplanted stem cells will undergo self-renewal and multipotent differentiation, which could result in regeneration of the sphincter and its neural connections.

Regulatory Status

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

- In 1993, Contigen (Allergan, Inc.), a cross-linked collagen, was approved. A supplemental approval in 2009 limited the device's indication to 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. The manufacturer of the product ceased production in 2011; no reason for discontinuation was provided to the public.
- In 1999, Durasphere (Advanced UroScience), pyrolytic carbon-coated zirconium oxide spheres, was approved.
- In 2004, Uryx (CR Bard), vinyl alcohol copolymer implants, was approved. In 2005, approval was given to market the device under the trade name Tegress. In 2007, Tegress was voluntarily removed from the market due to safety concerns.

- In 2005, Coaptite (BioForm Medical, Inc.), spherical particles of calcium hydroxylapatite, suspended in a gel carrier, was approved
- In 2006, Macroplastique (Uroplasty), polydimethylsiloxane, 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.

IV. RATIONALE

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Summary of Evidence

For individuals who have stress urinary incontinence 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. Studies have shown that cross-linked collagen improves the net health outcome (i.e., it is effective in some patients who failed conservative treatment with fewer adverse events than surgery), although this product is no longer commercially available. There is evidence that Food and Drug Administration (FDA) FDA-approved carbon-coated spheres, calcium hydroxylapatite, and polydimethylsiloxane have efficacy for treating incontinence and produce outcomes and have a safety profile similar to cross-linked collagen. The evidence is sufficient to determine qualitatively that the technology results in a meaningful 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 outcome measures 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 important to determine the durability of any treatment effect. The evidence is insufficient to determine the effects of the technology on health outcomes.

V. DEFINITIONS

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510(K) APPROVAL refers to section 510(k) of the Food, Drug and Cosmetic Act. Under 510(k), before a manufacturer can market a medical device in the United States, they must demonstrate to FDA's satisfaction that it is substantially equivalent (as safe and effective) to a device already on the market.

MIXED INCONTINENCE is a combination of stress and urge incontinence.

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OVERFLOW INCONTINENCE is characterized by small frequent voidings due to overfilling of the bladder or to a bladder with pathologically decreased volume.

PESSARY is a device inserted into the vagina to function as a support structure for the uterus.

STRESS INCONTINENCE is an involuntary loss of urine that occurs during physical activity, such as coughing, sneezing, laughing or exercise. This incontinence occurs as a result of weakened pelvic muscles that support the bladder and urethra, or because of malfunction of the urethral sphincter.

URGE INCONTINENCE is a condition characterized by a strong desire to urinate immediately before an involuntary bladder contraction with a loss of a large amount of urine.

VI. BENEFIT VARIATIONS

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The existence of this medical policy does not mean that this service is a covered benefit under the member's contract. Benefit determinations should be based in all cases on the applicable contract language. Medical policies do not constitute a description of benefits. A member's individual or group customer benefits govern which services are covered, which are excluded, and which are subject to benefit limits and which require preauthorization. Members and providers should consult the member's benefit information or contact Capital BlueCross for benefit information.

VII. DISCLAIMER

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Capital BlueCross medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. Capital BlueCross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

VIII. CODING INFORMATION

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Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Investigational; therefore, not covered:

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HCPCS Code	Description
L8605	Injectable bulking agent, dextranomer/hyaluronic acid copolymer implant, anal canal, 1 ml, includes shipping and necessary supplies

Investigational; therefore, not covered:

CPT Codes®								
0377T								

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Covered when medically necessary:

CPT Codes®								
51715								

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HCPCS Code	Description
L8603	Injectable bulking agent, collagen implant, urinary tract, 2.5 ml syringe, includes shipping and necessary supplies
L8606	Injectable bulking agent, synthetic implant, urinary tract, 1 ml syringe, includes shipping and necessary supplies

ICD-10-CM Diagnosis Code*	Description
N36.42	Intrinsic sphincter deficiency (ISD)
N36.43	Combined hypermobility of urethra and intrinsic sphincter deficiency
N39.3	Stress incontinence (female) (male)
N39.46	Mixed incontinence (urge and stress incontinence)

IX. REFERENCES

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X. POLICY HISTORY

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MP 4.012	**CAC 6/29/04**
	CAC 12/14/04
	CAC 1/31/06
	CAC 2/27/07
	CAC 1/29/08
	CAC 3/31/09
	CAC 3/30/10 Consensus Review
	CAC 4/26/11 Adopted BCBSA. Added statement that the use of periurethral bulking agents to treat urge urinary incontinence is considered investigational. Background/description regarding periurethral bulking agents was revised to reflect current available agents. Policy statements regarding carbon-coated spheres were revised as Tegress was previously withdrawn from the market. BCBSA criteria for periurethral bulking agents and transvaginal and transurethral radiofrequency tissue remodeling for

	urinary stress incontinence were adopted. A Medicare variation was added to the policy for collagen implants. Information related to EMGs and non-surgical/non-pharmacological urinary incontinence therapy related to diagnoses was removed from the policy.
	CAC 6/26/12 Consensus. No change to policy statements. Added BCBSA's Background /Description for Transvaginal and Transurethral Radiofrequency Tissue Remodeling for Urinary Stress Incontinence
	7/29/13 Admin coding review complete
	CAC 9/24/13 Minor. Policy title changed – formally titled Urinary Incontinence Treatment (Including Periurethral Bulking Agents). Added investigational statement "The use of perianal bulking agents to treat fecal incontinence is considered investigational". Extracted information regarding transvaginal and transurethral radiofrequency tissue remodeling for urinary stress incontinence and a separate policy created - MP 4.034 Transvaginal and Transurethral Radiofrequency Tissue Remodeling for Urinary Stress Incontinence. Added rationale section.
	CAC 7/22/14 Consensus review. No changes to the policy statements. References and rationale updated.
	CAC 7/21/15 Consensus review. Cross-linked collagen (Contigen®) is no longer available - no reason for discontinuation was provided to the public. Information removed from the policy. No other changes to the policy statements. Rationale and references updated. Coding reviewed.
	CAC 7/26/16 Consensus review. No change to policy statements. References and rationale reviewed. Coding reviewed**.**
	Admin update 1/1/17: Product variation section reformatted.
	CAC 9/26/17 Consensus. No change to policy statements. References and rationale updated. Coding Reviewed.
	1/1/18 Admin Update: Medicare variations removed from Commercial Policies.
	5/1/18 Coding reviewed. L8604 removed from policy.
	6/11/18 Consensus review. No change to policy statements. References updated. Rationale condensed.

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