
	
<b>Medical Policy</b>	
ARBenefits Approval: <Date>	Title: Periurethral Bulking Agents for the Treatment of Incontinence
Effective Date: 01/01/2012	Document: ARB0279
Revision Date:	
Code(s): 51715 Endoscopic injection of implant material into the submucosal tissues of the urethra and/or bladder neck  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	
Administered by: 	

## Public Statement:

Periurethral bulking agents are substances that are injected periurethrally to increase tissue bulk around the urethra as a treatment of stress incontinence. Improvement in stress incontinence is achieved by increasing the tissue bulk and thereby increasing resistance to the outflow of urine. ARBenefits covers injection of cross-linked collagen, carbon-coated spheres, or copolymers for this indication. The injection of Teflon®, autologous fat, or autologous ear chondrocytes is considered investigational and is not covered.

## Medical Policy Statement:

- 1) The use of cross-linked collagen, carbon-coated spheres, or copolymers is considered medically necessary and is covered to treat stress urinary incontinence in men and women.
- 2) The use of Teflon® or any other material is considered investigational and is not covered.

## Background:

Cross-linked collagen (e.g., Contigen) has been commercially available for many years, but recently the use of carbon-coated beads (e.g., Durasphere) has received approval by the U.S. Food and Drug Administration (FDA) as a periurethral bulking agent. The

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use of collagen is preceded by a skin test to rule out hypersensitivity. No such testing is required when carbon-coated beads are used. The substances may be injected over a course of several treatments until the desired effect is achieved. Since cross-linked collagen is slowly absorbed over time, symptoms may recur, requiring retreatment. The use of carbon-coated beads is thought to provide a more durable effect. Periurethral bulking agents have been widely used for incontinence in women, and their FDA-labeled indication is limited to their use in women. However, men have also been treated, most commonly those with post-prostatectomy incontinence.

Polytetrafluoroethylene (Teflon®) is another implant material that has been investigated but has not received FDA approval.

Periurethral bulking agents are recognized as treatment options for both men and women with stress incontinence. The 1996 Clinical Practice Guidelines for Urinary Continence in Adults, developed by the Agency for Health Care Policy and Research (AHCPR) concluded that periurethral collagen is curative in 32% of men and 62% of women. Success may be maximized in men by assessing outcome after 4 injections, and by focusing treatment on those with milder degrees of incontinence. Carbon-coated beads (Durasphere) are a recently FDA-approved alternative to cross-linked collagen. They are designed to provide a more durable effect. A double-blind randomized study comparing the Durasphere to Contigen was reported to the FDA as part of the FDA-approval process. At the end of the 12-month study period, the 2 devices reported equal effectiveness. There was also no difference in the number of treatments between the 2 groups, although the trial length of 12 months might not have been long enough to assess comparative durability. Results from this study were later published by Lightner and colleagues in 2001. The copolymer implant (Uryx) received FDA approval based on a study that randomized 237 women with stress urinary incontinence to undergo periurethral bulking with Uryx or to a “currently marketed absorbable bulking agent.” The effectiveness at 12 months was similar in the 2 groups. For example, 18.4% and 48.7% of those receiving Uryx reported that they were either dry or had improved by 1 grade respectively, compared to 16.5% and 53.2% in the control group. A repeat injection was necessary in 75% of these patients to achieve satisfactory results.

Autologous fat and autologous ear chondrocytes are other materials that have been used as bulking agents but have not demonstrated sustained effectiveness comparable to cross-linked collagen or carbon-coated beads. Autologous substances do not require FDA approval. In a randomized, double-blind clinical trial of 56 female patients comparing periurethral injections of autologous fat (treatment group) to saline (placebo group), Lee and colleagues found periurethral fat injections did not appear to be more efficacious than placebo for treating stress incontinence. At 3 months, only 6 of 27 patients (22.2%) in the treatment group and 6 of 29 (20.7%) in the placebo group were cured or improved. In addition, one death occurred as a result of a pulmonary fat embolism.

In another clinical trial of 32 female patients, Bent and colleagues reported 50% of patients remained dry for 12 months after receiving a single outpatient injection of

harvested autologous auricular cartilage. 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. Further study of the use of autologous ear chondrocytes is also warranted.

An updated Cochrane review of 12 trials (5 added since the prior review) found that greater symptomatic improvement was observed after surgery, but that this advantage needed to be balanced against higher risks (Keegan et al, 2007). The authors concluded that the moderate quality of the studies reviewed still provided an unsatisfactory basis for practice, but “pending further evidence, injection therapy may represent a useful option for short-term symptomatic relief amongst selected women with co-morbidity that precludes anesthesia – two or three injections are likely to be required to achieve a satisfactory result.” Another systematic review of various non-surgical treatments concluded (on the basis of only 4 randomized trials) that the results of injectable bulking agents were inconsistent (Shamilyan et al, 2008).

Calcium hydroxylapatite was found to have similar effects to collagen in an industry-sponsored multicenter randomized trial involving 231 women with stress urinary incontinence (Mayer et al, 2007). For the primary outcome measure, 83 patients treated with calcium hydroxylapatite and 57 control patients treated with collagen showed an improvement of one grade or more on the Stamey Urinary Incontinence Scale at 12-month follow-up. Similar results were obtained by intent-to-treat analysis, with non-inferiority of calcium hydroxylapatite to collagen for improvement of at least one Stamey Grade and decrease in pad weight of 50% or more.

In 2007, Strasser et al reported results of autologous cell therapy in 63 women with stress urinary incontinence in a randomized single-blind controlled trial. Using ultrasonic guidance, autologous myoblasts were injected into the rhabdosphincter, and fibroblasts (in a collagen suspension) were injected into the submucosa (n=42). The control group consisted of 21 women treated (on a single occasion) with endoscopically guided collagen for coaptation of the urethral wall and compression of the urethral lumen. Twelve-month follow-up showed that 90% of the patients in the experimental group were continent and required no pads in comparison with 10% of patients in the control group. The incontinence score decreased from a mean of 6 (totally incontinent) to 0 (totally continent) following autologous cell therapy. There was no mean decrease in the average incontinence score in the collagen group. The increase in thickness (from 2.0 to 3.4 mm) and contractility (from 0.5 to 1.6 mm) of the rhabdosphincter was found to be greater in the cell therapy group in comparison with patients treated with collagen alone (2.3 to 2.3 mm and 0.7 to 0.7 mm, respectively). Thickness of the urethra was not different between the groups. This is the first published study of autologous cell therapy; additional study with longer follow-up is needed to permit conclusions concerning the effect of this technology on health outcomes.

## References:

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Bent AE, Tutrone RT, McLennan MT, et al.(2001) Treatment of intrinsic sphincter deficiency using autologous ear chondrocytes as a bulking agent. *Neurourol Urodyn* 2001; 20(2):157-65.

Cespedes RD.(2000) Collagen injection or artificial sphincter for postprostatectomy incontinence: Collagen. *Urology* 2000; 55:5-7.

Chapple CR, Haab F, Cervigni M et al.(2005) An open, multicentre study of NASHA/Dx Gel (Zuidex) for the treatment of stress urinary incontinence. *Eur Urol* 2005; 48(3):488-494.

Collagen Implantation for the Treatment of Urinary Incontinence. 1994 Blue Cross Blue Shield Association Technology Evaluation Center Assessment; Tab 14.

Corcos J, Collet JP, Shapiro S et al.(2005) Multicenter randomized clinical trial comparing surgery and collagen injections for treatment of female stress urinary incontinence. *Urology* 2005; 65(5):898-904.

Fianu-Jonasson A, Edwall L, Wiberg MK et al.(2006) Magnetic resonance imaging to evaluate NASHA/Dx gel (Zzuidex) for stress urinary incontinence. *Int J Clin Pract* 2006; 60(10):1181-1186.

Herschorn S, Radomski SB, Steele DJ.(1992) Early experience with intraurethral collagen injections for urinary incontinence. *J Urol* 1992; 148:1797-1800.

Hurtado e, McCrery R, Appell R et al.(2007) The safety and efficacy of ethylene vinyl alcohol copolymer as an intra-urethral bulking agent in women with intrinsic urethral deficiency. *int Urogynecol J Pelvic Floor Dysfunct* 2007; 18(8): 869-873.

Keegan PE, Atiemo K, Cody J et al.(2007) Periurethral injection therapy for urinary incontinence in women. *Cochrane Database Syst Review* 2007; (3):CD003881.

Kieswetter H, Fischer M, Wober L, Flamm J.(1992) Endoscopic implantation of collagen (GAX) for the treat-ment of urinary incontinence. *Br J Urol* 1992; 69:22-5.

Lee PE, Kung RC, Drutz HP.(2001) Periurethral autologous fat injection as treatment for female stress urinary incontinence: a randomized double-blind controlled trial. *J Urol* 2001; 165(1):153-8.

Lightner D, Calvosa C, Andersen R, et al.(2001) A new injectable bulking agent for treatment of stress urinary incontinence: results of a multicenter, randomized, controlled, double blind study of Durasphere. *Urology* 2001; 58(1):12-5.

Litwiller SE, Kim KP, Fone PD, et al.(1996) Post-prostatectomy incontinence and the artificial urinary sphincter: A long-term study of patient satisfaction and criteria for success. *J Urol* 1996; 156:1976-80.

Mayer RD, Dmochowski RR, Appell RA et al.(2007) Multicenter prospective randomized 52-Week trial of calcium hydroxylapatite versus bovine dermal collagen for treatment of stress urinary incontinence. Urology 2007; 69(5):876-880.

Shamliyan TA, Kane RL, Wyman J et al.(2008) Systematic review: randomized, controlled trials of nonsurgical treatments for urinary incontinence in women. Ann Intern Med 2008; 148(6): 459-473.

Strasser H, Marksteiner R, Margreiter E et al.(2007) Autologous myoblasts and fibroblasts versus collagen for treatment of stress urinary incontinence in women: a randomised controlled trial. Lancet 2007; 369(9580):2179-2186.

Stricker P, Haylen B.(1993) Injectable collagen for type 3 female stress incontinence: the first 50 Australian patients. Med J Aust 1993; 158:89-91.

U.S. Food and Drug Administration. Summary of safety and effectiveness data for Coaptite. Accessible at <http://www.fda.gov/cdrh/pdf4/P040047a.pdf>. Accessed 4/9/2008.

U.S. Food and Drug Administration. Summary of safety and effectiveness data for Macroplastique. Accessible at <http://www.fda.gov/cdrh/pdf4/P040050a.pdf>. Accessed 4/9/2008.

Urinary Incontinence in Adults: Clinical Practice Guideline. AHCPR 1992 Pub # 92-0038.

Uryx.(2003) FDA Summary of Safety and Effectiveness. <http://www.fda.gov/cdrh/PDF3/p030030b.pdf>.; 2003.

Wan J, McGuire EJ, Bloom DA, et al.(1992) The treatment of urinary incontinence in children using glutaraldehyde cross-linked collagen. J Urol 1992; 148:127-30.

## Application to Products

This policy applies to ARBenefits. Consult ARBenefits Summary Plan Description (SPD) for additional information.

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