Coverage Policy

Cigna covers ANY of the following injectable bulking agents as medically necessary for the treatment of adult stress urinary incontinence (SUI) secondary to intrinsic sphincter deficiency (ISD) when there is failure, contraindication or intolerance to at least 12 months of conservative medical management:

- Glutaraldehyde cross-linked [GAX] bovine collagen (e.g., Contigen®) in men or women
- Carbon-coated zirconium oxide particles (e.g., Durasphere™), calcium hydroxylapatite [CaHA] particles (e.g., Coaptite®), or silicone elastomer (e.g., Macroplastique®) in women

Cigna covers the endoscopic injection of Deflux® as medically necessary for the treatment of severe vesicoureteral reflux (i.e., stage II–IV) in children age one year or older.

Cigna does not cover any other injectable urinary bulking agent other than those specified above as they are considered experimental, investigational or unproven.

Cigna does not cover injectable bulking agents (e.g., Solesta®) for the treatment of fecal incontinence as they are considered experimental, investigational or unproven.
General Background

Urinary incontinence is the involuntary loss of urine. It is not a disease but rather a symptom that can be caused by a wide range of conditions. There are several types of incontinence:

- **Stress incontinence** is the most common type of leakage. This occurs when urine is lost during activities such as walking, aerobics or even sneezing and coughing. The primary causes are urethral sphincter weakness "intrinsic sphincter deficiency" or a hypermobile urethra. "Urethral hypermobility" occurs when there is weakness of pelvic floor and poor support of the vesicourethral sphincter unit. The proximal urethra can be displaced outside the abdominal pressure zone during straining.

- **Urge incontinence**, often referred to as "overactive bladder," is another form of leakage. This can happen when a person has an uncontrollable urge to urinate but cannot reach the bathroom in time.

- **Overflow incontinence** occurs when the bladder is full, is unable to empty and yet leaks. Frequent small urinations and constant dribbling are symptoms. This is rare in women and more common in men with a history of surgery or prostate problems.

- **Functional incontinence** is the inability to access a proper facility or urinal container because of physical or mental disability.

- **Mixed incontinence** refers to a combination of types of incontinence; most commonly stress and urge incontinence.

**Stress Urinary Incontinence (SUI)**

If conservative medical treatments such as bladder training, pelvic floor muscle exercises, biofeedback, or medication fail to improve SUI, additional intervention may be necessary. Injectable therapy using bulking agents composed of synthetic materials, bovine collagen, or an autologous substance augments the urethral wall and increases urethral resistance to urinary flow. Injection of bulking agents to treat a dysfunctional urethra is a minimally invasive method of correcting intrinsic sphincteric deficiency (ISD) that results in SUI. ISD may be caused by aging or scarring.

Bulking agents are materials that are injected into tissue surrounding the urethra to help keep the urethra closed and reduce urine leakage. A bulking agent procedure — usually done in a doctor's office — requires minimal anesthesia and takes about five minutes. Bulking up the bladder neck with particulate matter effectively closes the lumen of the urethra, which improves urethral coaptation and restores the mucosal seal mechanism of continence. The downside of the procedure is that most available bulking agents lose their effectiveness over time, and repeat injections are usually needed every six to 18 months. New bulking agents are being developed, as well as new ways to make the injection process easier and more efficient. The standard method of injecting a bulking agent is through a needle, which is inserted in different positions with the assistance of a cystoscope. Treatment-related adverse events are uncommon and relatively minor, the most common being dysuria, urinary urgency, transient urinary retention and acute (e.g., < seven days) urinary retention. Injectable agents are contraindicated in the presence of acute cystitis, urethritis, acute genitourinary infection, and bladder neck or urethral stricture. They should not be injected into blood vessels. Materials used as bulking agents for stress urinary incontinence include:

- glutaraldehyde cross-linked [GAX] bovine collagen (i.e., Contigen®).
- carbon-coated zirconium oxide particles (i.e., Durasphere™)
- calcium hydroxylapatite [CaHA] particles (i.e., Coaptite®)
- silicone elastomer/polydimethylsiloxane (i.e., Macroplastique®)
- polytetrafluoroethylene (PTFE; Teflon)

Autologous Fat: Before the FDA approved collagen for use, fat injections were used to treat intrinsic sphincter deficiency (ISD) by bulking up the urethra. The short-term result of periurethral fat injection is extremely good. Over time, however, the injected adipocytes tend to be phagocytized by the patient’s own body. This high degree of fat absorption is the major detriment to long-term cure.

**U.S. Food and Drug Administration (FDA):** Contigen (glutaraldehyde cross-linked [GAX] bovine collagen) (C. R. Bard, Covington, GA, USA) received a premarket approval (PMA) in 1993 from the FDA. Once injected, this bovine collagen begins to degrade within 12 weeks and completely degrades in 9–19 months. One month before receiving the first treatment, the patient must undergo a skin test to exclude hypersensitivity. Per 2009
PMA update, the device was modified and is marketed under the trade name Contigen Bard Collagen Implant and is indicated for use only in the treatment of urinary incontinence due to intrinsic sphincter deficiency (ISD) that may be helped by a locally injected bulking agent. Contigen implant therapy should be initiated only in patients who have shown no improvement in their incontinence for at least 12 months.

Durasphere (carbon bead particles) (Carbon Medical Technologies, St. Paul, MN, USA) was approved by the FDA in 1999 for use in treating ISD in women age 21 and over. The use of carbon-coated zirconium oxide particles is restricted to women, as the studies that were submitted with the PMA application showed no improvement in the small number of male and child participants. Skin testing is not required prior to the use of this product. In 2002 there were bead modifications and a trade name revision to Durasphere EXP, also indicated for use in the treatment of adult women with stress urinary incontinence (SUI) due to ISD.

Coaptite (calcium hydroxylapatite) (BioForm Medical, Inc., San Mateo, CA, USA) was granted PMA by the FDA in November 2005. Coaptite is an injectable, sterile implant composed of spherical particles of calcium hydroxylapatite (CaHA), suspended in an aqueous based gel carrier. The gel carrier is composed of sodium carboxymethyl cellulose, sterile water for injection, and glycerin. It is indicated for soft tissue augmentation in the treatment of SUI due to ISD in adult females. It is contraindicated in patients with 1) significant history of urinary tract infections without resolution, or 2) current or acute conditions of cystitis or urethritis, or 3) fragile urethral mucosal lining.

Macroplastique Implants (silicone elastomer/polydimethylsiloxane) (Uroplasty, Inc., Minnetoka, MN, USA) was granted PMA by the FDA in October 2006. Macroplastique is a permanently implanted, injectable bulking agent composed of polydimethylsiloxan particles suspended in a polyvinylpyrrolidone (PVP) carrier gel. It is indicated for transurethral injection in the treatment of adult women diagnosed with SUI primarily due to ISD. Macroplastique is contraindicated in patients with 1) acute urogenital tract inflammation or infection, or 2) fragile urethral mucosal lining (e.g., post-radiation therapy, post-surgery to the bladder neck).

Teflon: Because of the risk of migration, polytetrafluoroethylene (PTFE; Teflon) is not approved by the US Food and Drug Administration (FDA) for treatment of female SUI.

Tegress™ (C.R. Bard, Covington, GA, USA) formerly known as URYX® (Genyx Medical, Inc., Aliso Viejo, CA) received PMA from the FDA in December 2004 for the treatment of SUI due to ISD in adult women. It is made of ethylene vinyl alcohol (EVOH) copolymers. Bard voluntarily discontinued sales of Tegress™ in 2007 due to reports of up to 37% erosion rates.

Bulkamid® (Contura International, Denmark), Zuidex (Q-MED Uppsala, Sweden) and Vantris (Promedon, Cordoba, Argentina) urethral bulking agents are currently not approved by the FDA. Polytetrafluoroethylene (PTFE, Teflon®) and autologous myoblasts are not addressed by the FDA as urinary bulking agents.

**Literature Review:** The safety and clinical utility of most FDA-approved urethral bulking agents are well-supported in the peer-reviewed scientific literature. While several agents have received approval for use through the FDA, their clinical efficacy has not been proven in all patient populations (e.g., women, men and/or children). Several manufacturers have printed warnings on their package inserts that their product has not been tested in women who are pregnant, in children or men. While some studies have included males in their study population, outcomes do not support the use of most agents for the treatment of male urinary incontinence. At this time, collagen is the only injectable agent that has been approved for use in men. Collagen injection has been used in the treatment of stress urinary incontinence (SUI) since 1993. Studies in the peer-reviewed scientific literature support the use of Contigen (collagen) injections for SUI with 50% - 60% success rates (social continence, 24-hour dry pad test) at 12-24 months follow-up. Studies include men and women. Studies address SUI caused by intrinsic sphincter deficiency (ISD) only, or both ISD and urethral hypermobility. Although collagen injection is considered a safe and effective procedure, most patients need additional treatment sessions to achieve and maintain improvement or cure (Corcos, et al., 2005; Winters, et al., 2000; Smith, et al., 1998; Smith, et al., 1997).

Ghoniem et al. (2012) conducted a systematic review and meta-analysis of the evidence (n= 23 cohort studies/958 patients) on the safety and effectiveness of Macroplastique® (polydimethylsiloxane injection) SUI. Improvement rates were 75 % in the short-term, 73 % in the mid-term (6-18 months), and 64 % in the long-term
(>18 months). Cure/dry rates were 43 %, 37 %, and 36 % during the same respective follow-up periods. No serious adverse events were reported. According to the authors, this meta-analytic evidence is supportive of Macroplastique as a safe and effective urethral bulking agent for treating with SUI primarily due to ISD.

A Cochrane review by Kirchin et al. (2012) assessed the effects of periurethral or transurethral injection therapy on the cure or improvement of urinary incontinence in women in randomized controlled trials (n=14 studies/2004 subjects). The limited data were not suitable for meta-analysis. Trials were small and generally of moderate quality. Of the 14 trials, eight compared different agents and all results had wide confidence intervals suggesting uncertainty. Silicone particles, calcium hydroxylapatite, ethylene vinyl alcohol, carbon spheres and dextranomer hyaluronic acid combination gave improvements which were not shown to be more or less efficacious than collagen. It was summarized that no clear-cut conclusions could be drawn from trials comparing agents. Insufficient evidence was found to show superiority of mid-urethral or bladder neck injection. Further comparative randomized trials with long term follow-up, involving a placebo or conservative treatment arm are required before injection therapy can be recommended as a standard first-line treatment for stress incontinence.

Ghoniem et al. (2009) randomized 247 patients (122 received Macroplastique; 125 received Contigen). The Contigen group served as the control. At 12 months, the Macroplastique group the dry/cure rate was 36.9% compared to 24.8% in the control group (p <0.05). In the Macroplastique and control groups the 1-hour pad weight decrease was 25.4 and 22.8 ml from baseline (p = 0.64), and the mean improvement in Urinary Incontinence Quality of Life Scale score was 28.7 and 26.4 (p = 0.49), respectively.

Mayer et al. (2007) compared the safety and effectiveness of Coaptite (calcium hydroxylapatite) to Contigen (collagen) in a randomized controlled trial (n=231). Up to five injections were performed in the first six months of the trial. At 12 months, 63.4% of Coaptite patients compared to 57.0% of Contigen patients showed improvement of ≥1 incontinence grade (not statistically significant). Most of the Coaptite and Contigen patients received two to three injections, and the mean number of injections was similar for the Coaptite and Contigen; however, a significantly greater percentage of Coaptite patients (38%) than collagen patients (26.1%) had only one injection (p=0.03). No statistically significant differences were found in the number of patients requiring greater than one injection of the test materials.

A randomized controlled trial (n=45) compared the safety and clinical utility of Macroplastique (silicone elastomer) to pubovaginal sling procedure in the treatment of female SUI (Maher, et al., 2005). Within each group, there was a significant improvement in outcome as documented by the 1-hour pad test and validated urinary incontinence questionnaires. Macroplastique is associated with reduced morbidity when compared to the sling, including significantly decreased operating time, blood loss, hospital stay and a quicker return to normal activity. While the subjective, patient-determined and objective evaluations were all greater in the sling group, the objective evaluation was the only parameter in which the sling demonstrated a statistically superior outcome to the Macroplastique in the short term (81% versus 9%).

Anderson (2002) also conducted a randomized controlled trial (n=46), with a longer average length of follow-up of 32.3 months. A total of 80% of Durasphere patients and 62% of Contigen patients demonstrated an improvement of ≥1 continence grade at 2.6 and 2.8 years, respectively. This difference was not statistically significant.

A randomized controlled trial (n=129) compared the safety and clinical utility of Durasphere (carbon-coated zirconium oxide beads) to Contigen (collagen) in the treatment of SUI and found the two materials comparable with respect to the improvement in continence grade and pad weight testing at 12 months (Lightner, et al., 2001). Specifically, when examined one year after the date of the last treatment, 49 (80.3%) of the 61 women treated with Durasphere showed improvement of one continence grade or more compared to 47 (69.1%) of 68 women treated with bovine collagen (p=0.162, this difference was not statistically significant).

**Professional Societies/Organizations:** In a systematic review by the International Consultation on Incontinence on Surgical Treatment of Stress Incontinence in Men, Herschorn et al. (2010) states the following regarding urethral bulking agents: Bulking agents remain the most minimally invasive treatment for post-RP incontinence after conservative measures. All agents for which there is peer-reviewed data available, show only modest success rates with low cure rates. Effects tend to deteriorate over time. It remains to be seen if improvements in outcomes can be achieved with alternative agents, or if the concept of urethral bulking has achieved its maximal benefit with the agents available now.
The American College of Obstetricians and Gynecologists (ACOG) guideline entitled ‘Urinary incontinence in women’ lists the following “Major Recommendations”:

Level B evidence:
- Bulking agents are a relatively noninvasive method of treatment for stress incontinence and can be used in women for whom any form of operative treatment is contraindicated.

Levels of Recommendations:
Level A — Recommendations are based on good and consistent scientific evidence.
Level B — Recommendations are based on limited or inconsistent scientific evidence.
Level C — Recommendations are based primarily on consensus and expert opinion (ACOG, 2005).

**Vesicoureteral Reflux (VUR)**

VUR is the abnormal flow of urine from the bladder backwards towards the kidneys. Most commonly a condition of infancy and childhood, VUR increases the risk of urinary tract infections and can lead to kidney damage. Children with primary VUR are born with a defect in the valve that normally prevents urine from flowing backward from the bladder into the ureters. Some children with primary outgrow the condition. Secondary vesicoureteral reflux is due to a urinary tract blockage, often caused by infection. Treatment for both primary and secondary VUR is aimed at preventing kidney damage. Depending on the severity of the condition, treatment options include watchful waiting, medication and surgery. Surgery is typically reserved for those children for whom antibiotics are not successful. However, surgery may be a first line therapy option for grades IV and V or when a quicker, more definitive treatment than medication is appropriate.

In endoscopic surgery, a bulking agent (e.g., Deflux®, Oceana Therapeutics, Inc., Edison, NJ, USA) is injected around the opening of the affected ureter to try to strengthen the valve's ability to close properly. This method is minimally invasive and compared to open surgery and presents fewer surgical risks. This procedure also requires general anesthesia, but generally can be performed as outpatient surgery. The American Urological Association states "the significantly lower morbidity associated with the use of Deflux, compared to open surgery, indicates Deflux must be considered as an important option in VUR management. The choice of management options remains with the informed family and the physician, based upon multiple factors including age, sex, reflux grade, voiding patterns, risk of renal injury, and parental preferences" (2007).

**U.S. Food and Drug Administration (FDA):** At the present time, Deflux (Oceana Therapeutics, Inc., Edison, NJ, USA) is the only FDA-approved injectable bulking agent for use in vesicoureteral reflux (VUR). Granted PMA by the FDA in September 2001, it is cross-linked dextran (dextranomer) microspheres in a carrier gel. It is intended for use in treating children age one year and over diagnosed with vesicoureteral reflux (stage II–IV). It cannot be used in children with a urinary tract infection.

**Literature Review: Vesicoureteral Reflux (VUR):** The overall success rate reported by different groups of authors for use of Deflux ranged between 68% and 92% depending mainly on the VUR grade (Chertin and Kocherov, 2009). Study results indicate that VUR can be treated successfully with Deflux, producing positive short- and long-term outcomes and providing an alternative to antibiotics or open surgery (Stenberg, et al., 2007; Puri, et al., 2006; Capozza, et al., 2002; Capozza, et al., 2001; Lackgren, et al., 2001).

A meta-analysis of the literature on endoscopic therapy for vesicoureteral reflux was conducted by Elder et al. (2006). This analysis included the treatment of 5527 patients. The articles dealt with polytetrafluoroethylene (PTFE, Teflon), collagen, dextranomer/hyaluronic acid (Deflux), polydimethylsiloxane (Macroplastique), chondrocytes, blood and 2 or more injectables. In the database 47 articles (75%) pertained to children, 6 (10%) adults, and 10 (16%) children and adults. The number of studies of patients, and percent of reflux resolution by bulking agent was as follows:

- Teflon: 33 / 361 / 66.86%
- Collagen: 10 / 947 / 56.86%
- Deflux: 3 / 385 / 68.71%
- Macroplastique: 8 / 347 / 76.46%
• Chondrocytes: 1 / 47 / 50.48%

Overall, following one treatment, the reflux resolution rate (by ureter) for grades I and II reflux was 78.5%, grade III 72%, grade IV 63% and grade V 51%. If the first injection was unsuccessful, the second treatment had a success rate of 68%, and the third treatment 34%. The aggregate success rate with 1 or more injections was 85%. The success rate was similar among children and adults. It should be noted that relatively few studies included the incidence of urinary tract infection (UTI) in patients undergoing endoscopic therapy. The authors stated that further study of the rates of UTI and pyelonephritis after endoscopic and open antireflux surgery is necessary. The authors concluded that future studies pertaining to endoscopic therapy should include data on rates of UTI and renal scarring, with prolonged follow-up (Elder, et al., 2006).

Professional Societies/Organizations: The American Urological Association (AUA) Policy Statement on Use of Deflux® in the Management of Vesicoureteral Reflux states “It is the current position of the American Urological Association that endoscopic injection of the dextranomer/hyaluronic compound Deflux is an option in the management of pediatric vesicoureteral reflux (VUR). The absence of inclusion of Deflux in the 1997 Pediatric Reflux Guidelines simply reflects the fact that it had not been introduced at that time and therefore could not have been evaluated. The contention that Deflux has not been proven to reduce urinary infections associated with reflux is inappropriate to the same extent that no other treatment modality has been shown to reduce all urinary tract infections. The resolution of reflux has been shown to reduce the incidence of pyelonephritis. Therefore to the extent that Deflux can correct VUR, it will reduce the incidence of pyelonephritis. The significantly lower morbidity associated with the use of Deflux, compared to open surgery, indicates Deflux must be considered as an important option in VUR management. The choice of management options remains with the informed family and the physician, based upon multiple factors including age, sex, reflux grade, voiding patterns, risk of renal injury, and parental preferences. To attempt to dictate specific treatment modality based upon concrete evidence is impossible based upon the current state of evidence. Any claim that current evidence can guide such a decision reflects a lack of understanding of the state of current evidence. As more evidence emerges, selection of specific therapy for specific patients may become more appropriate. At present, Deflux must be considered an option in the care of the pediatric patient with VUR” (October 2007).

The AUA Management and Screening of Primary Vesicooureteral Reflux in Children Guideline (Peters, et al., 2010) states the following recommendation under Management of vesicooureteral reflux in the child over one year of age: “Recommendation: It is recommended that in patients receiving continuous antibiotic prophylaxis with a febrile breakthrough urinary tract infection be considered for open surgical ureteral reimplantation or endoscopic injection of bulking agents for intervention with curative intent.”

In general, there is limited evidence to support polytetrafluoroethylene (PTFE, Teflon) or autologous myoblasts injections or other non-FDA-approved agents, for use in SUI; or agents other than Deflux for use in VUR; or Deflux for use in SUI (Kotb, et al., 2009; Chertin and Kocherov, 2009; Dyer, et al., 2007; Yucel, et al., 2007; Lottmann, et al., 2006; Chapple, et al., 2005).

Fecal Incontinence
Fecal incontinence is the inability to control ones bowel movements in someone who is older than 4 years old. Common causes of fecal incontinence include constipation, diarrhea, and muscle or nerve damage. Fecal incontinence may be due to a weakened anal sphincter associated with aging or to damage to the nerves and muscles of the rectum and anus from giving birth. Treatment may include dietary changes, medications, special exercises to help better control the bowels, injection of bulking agents, or surgery.

U.S. Food and Drug Administration (FDA): Solesta® (Oceana Therapeutics, Inc., Edison, NJ, USA) received FDA-approval (P100014) in May 2011. It is approved for the treatment of fecal incontinence in patients 18 years and older who have failed conservative therapy (e.g., diet, fiber therapy, anti-motility medications). This product was developed under the name “NASHA/Dx Fecal.” Solesta is a sterile, viscous gel contained in a disposable 1 mL assembled glass syringe with a standard luerlock fitting. Solesta consists of dextranomer microspheres, 50 mg/mL, and stabilized sodium hyaluronate, 15 mg/mL, in phosphate buffered 0.9 % sodium chloride solution. Deflux, is the same material as Solesta.
Literature Review: Fecal incontinence: There is insufficient evidence in the peer-reviewed scientific literature to demonstrate long term safety and clinical utility of Solesta for fecal incontinence. There is a paucity of studies evaluating other bulking agents (e.g., Coaptite) for fecal incontinence.

A randomized controlled trial was conducted to compare injection of dextranomer in stabilized hyaluronic acid with a sham for treatment of fecal incontinence (Graf, et al., 2011). Patients were eligible for inclusion if they were aged 18–75 years, had a Cleveland clinic Florida fecal incontinence score (CCFIS) of 10 or higher and at least four recorded incontinence episodes in two weeks, had symptoms for at least 12 months, had failure of medically supervised conservative treatment (at least one of dietary modification, fiber supplements, or loperamide hydrochloride treatment) ending at least 2 weeks before the screening period, were able to understand and comply with the requirements of the study, and were available for follow-up. A total of 206 adults were randomized assigned to receive NASHA Dx (n=136) or sham treatment (n=70). Of the NASHA Dx group, 132 were analyzed at six months, and 125 analyzed at 12 months. In the sham group, 65 were analyzed at six months. After 6 months, the trial was unmasked, and patients in the sham treatment group were offered active treatment and were thereafter excluded from further analysis. Data from the first 6 months were used to assess the effect of active treatment compared with sham treatment. 12-month data from individuals in the active treatment group were used to assess the durability of injected NASHA Dx. The primary endpoint was response to treatment based on the number of incontinence episodes. A 50% or greater reduction in the number of incontinence episodes was noted in 71 patients in the active treatment group (52%) compared with 22 (31%) in the sham treatment group (p=0.0089), this is statistically significant. However, the median decrease in number of incontinence episodes was not significantly greater in the active treatment group than in the sham treatment group at both three months and 6 months. Change in CCFIS compared with baseline did not differ between treatment groups at 3 months or at 6 months. Recorded were 128 treatment-related adverse events, of which two were serious (one rectal abscess and one prostatic abscess). Small sample size and short term follow-up are limitations of this study.

Dodi et al. (2010) conducted a prospective observational study, treating 115 patients with fecal incontinence (FI) with NASHA/Dx gel. Of the 115 patients treated with NASHA/Dx gel, a total of 14 patients withdrew or were lost to follow-up at 6 months (n = 101), and additional 10 patients withdrew or were lost to follow-up at 12 months (n = 91). One month after the first treatment visit, the patients were offered retreatment of up to 4 treatments. The number of FI episodes per 24 hours was recorded in the diaries. Fever was fairly common after treatment. A total of 7% of patients reported pyrexia that was assessed by the investigator as related to treatment. A total of 6 cases of anorectal abscess were reported in the study. All of these events resolved after treatment. Results included a ≥50% reduction from baseline in the number of FI episodes in 57.1% of patients at 6 months, and 64.0% at 12 months. The reduction from baseline in number of FI episodes, recorded in the 28-day diary, was statistically significant at both 6 months (p<.001) and 12 months (p<.001) after last treatment. Limitations of this study include small sample size and no comparison group.

A Cochrane systematic review (n= 4 RCTs/ 176 patients) by Maeda et al. (2010) evaluated perianal injectable bulking agents as treatment for fecal incontinence in adults. Most studies reported a short term benefit from injections regardless of the material used as outcome measures improved over time. A silicone biomaterial was found to provide some advantages and was safer in treating fecal incontinence than carbon-coated beads in the short term. There were also short term benefits from injections delivered under ultrasound guidance compared to digital guidance. The silicone biomaterial did not demonstrate clinical benefit compared to control injection of normal saline. Within the available data, the authors found no reliable evidence for effectiveness of one treatment over another in improving fecal incontinence. It was noted that “a definitive conclusion cannot be drawn regarding the effectiveness of perianal injection of bulking agents for fecal incontinence due to the limited number of identified trials together with methodological weaknesses. Larger well-designed trials with adequate numbers of subjects using reliable validated outcome measures are needed to allow definitive assessment of the treatment for both effectiveness and safety” (Maeda, et al., 2010). A 2013 update to this Cochrane review included one additional trial (n=5 RCTs/382 patients). Similar conclusions were made by the authors were similar in that although “one large randomised controlled trial has shown that this form of treatment using dextranomer in stabilised hyaluronic acid (NASHA Dx) improves continence in the short term, the number of identified trials was limited and most had methodological weaknesses” (Maeda, et al., 2013).

Luo et al. (2010) conducted a systematic review on the efficacy and safety of injectable bulking agents for fecal incontinence (FI) and concluded “Currently there is little evidence for the effectiveness of injectable bulking agents in managing passive FI.”
**Professional Societies/Organizations:** The American Society of Colon and Rectal Surgeons (ASCRS) Practice parameters for the treatment of fecal incontinence (2007) notes that a surgical option includes injectable therapy (silicone biomaterial, carbon-coated beads). The guideline states when passive fecal incontinence caused by internal sphincter dysfunction is the predominant symptom, injectable therapy seems to be effective and safe, although its long-term efficacy has yet to be defined. Level of Evidence: II; Grade of Recommendation: B.

Levels of Evidence
I. Meta-analysis of multiple well-designed, controlled studies, randomized trials with low false-positive and low false-negative errors (high power)
II. At least one well-designed experimental study; randomized trials with high false-positive or high false negative errors or both (low power)
III. Well-designed, quasi-experimental studies, such as nonrandomized, controlled, single-group, preoperative/postoperative comparison, cohort, time, or matched case-control series
IV. Well-designed, nonexperimental studies, such as comparative and correlational descriptive and case studies
V. Case reports and clinical examples

Grades of Recommendations
A. Evidence of Type I or consistent findings from multiple studies of Type II, III, or IV
B. Evidence of Type II, III, or IV and generally consistent findings
C. Evidence of Type II, III, or IV but inconsistent findings
D. Little or no systematic empirical evidence

**Use Outside of the US**
The National Institute for Health and Clinical Excellence (NICE) and the National Collaborating Centre for Women’s and Children’s Health Guideline on urinary incontinence in women (September, 2013) notes that intramural bulking agents (glutaraldehyde cross-linked collagen, silicone, carboncoated zirconium beads or hyaluronic acid/dextran copolymer) should be considered for the management of SUI if conservative management has failed. Women should be made aware of the following:

- repeat injections may be required to achieve efficacy
- efficacy diminishes with time
- efficacy is inferior to that of retropubic suspension or sling.

Autologous fat and polytetrafluoroethylene used as intramural bulking agents are not recommended for the treatment of SUI.

The NICE guidance on the use of intramural urethral bulking procedures for SUI in women (November 2005) states “Current evidence on the safety and short-term efficacy of intramural urethral bulking procedures for stress urinary incontinence is adequate to support the use for these procedures provided that normal arrangements are in place for clinical governance and for audit or research.”

The NICE guidance on the use of injectable bulking agents for fecal incontinence states that the “Current evidence on the safety and efficacy does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research, which should take place in the context of a clinical trial or formal audit protocol that includes information on well-defined patient groups” (NICE, 2007).

**Summary**
Certain injectable bulking agents have been proven effective in treating stress urinary incontinence (SUI) due to intrinsic sphincter deficiency (ISD) in patients who meet specific selection criteria. Although the long-term efficacy of these agents is not known, studies have shown that the use of an injectable bulking agent may provide relief (improvement of one continence grade or more) of ISD in individuals’ refractory to conservative therapy in 50-80% of patients.
Studies of children treated for severe vesicoureteral reflux (VUR) (grades, II–IV) with Deflux injections have shown this bulking agent to be a safe and effective alternative to antibiotic prophylaxis or open surgical repair. Evidence in the peer-reviewed scientific literature demonstrating the long term safety and clinical utility of bulking agents for fecal incontinence including Solesta, is lacking. Well-designed, long-term trials are needed and the role of this technology in the treatment of fecal incontinence has not yet been demonstrated.

There is insufficient evidence to support the use of bulking agents for the treatment of stress urinary incontinence (SUI) or vesicoureteral reflux (VUR) other than those specified above (e.g., the use of polytetrafluoroethylene [PTFE, Teflon] or autologous myoblasts injections or other non-FDA-approved agents for SUI; the use of bulking agents other than Deflux for VUR; the use of Deflux for SUI).

### Coding/Billing Information

**Note:**
1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement

**Collagen/Carbon-coated Zirconium Oxide/Calcium Hydroxylapatite/Silicone Elastomer Agents:**

**Covered when medically necessary:**

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<tr>
<th>CPT® Codes</th>
<th>Description</th>
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<td>51715</td>
<td>Endoscopic injection of implant material into the submucosal tissues of the urethra and/or bladder neck</td>
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<tr>
<td>52327</td>
<td>Cystourethroscopy (including ureteral catheterization); with subureteric injection of implant material</td>
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<tr>
<th>HCPCS Codes</th>
<th>Description</th>
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<td>L8603</td>
<td>Injectable bulking agent, collagen implant, urinary tract, 2.5 ml syringe, includes shipping and necessary supplies</td>
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<tr>
<td>L8606</td>
<td>Injectable bulking agent, synthetic implant, urinary tract, 1 ml syringe, includes shipping and necessary supplies</td>
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<tr>
<th>ICD-9-CM Diagnosis Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>599.82</td>
<td>Intrinsic (urethral) sphincter deficiency (ISD)</td>
</tr>
<tr>
<td>625.6</td>
<td>Female stress incontinence</td>
</tr>
<tr>
<td>788.32</td>
<td>Stress incontinence, male</td>
</tr>
<tr>
<td>788.33</td>
<td>Mixed incontinence urge and stress (male)/(female)</td>
</tr>
</tbody>
</table>

**Experimental/Investigational/Unproven/Not Covered:**

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>All other codes</td>
<td></td>
</tr>
</tbody>
</table>

**Deflux®:**

**Covered when medically necessary:**

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>51715</td>
<td>Endoscopic injection of implant material into the submucosal tissues of the</td>
</tr>
<tr>
<td>HCPCS Codes</td>
<td>Description</td>
</tr>
<tr>
<td>-------------</td>
<td>-------------</td>
</tr>
<tr>
<td>L8604</td>
<td>Injectable bulking agent, dextranomer/hyaluronic acid copolymer implant, urinary tract, 1 ml, includes shipping and necessary supplies</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-9-CM Diagnosis Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>593.70</td>
<td>Vesicoureteral reflux; unspecified or without reflux nephropathy</td>
</tr>
<tr>
<td>593.71</td>
<td>Vesicoureteral reflux; With reflux nephropathy, unilateral</td>
</tr>
<tr>
<td>593.72</td>
<td>Vesicoureteral reflux; With reflux nephropathy, bilateral</td>
</tr>
<tr>
<td>593.73</td>
<td>Vesicoureteral reflux; With reflux nephropathy NOS</td>
</tr>
</tbody>
</table>

**Bulking Agents for Fecal Incontinence (e.g., Solesta®):**

Experimental/Investigational/Unproven/Not Covered when used to report the Solesta® product or the administration of Solesta®:

<table>
<thead>
<tr>
<th>CPT* Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>46999</td>
<td>Unlisted procedure, anus</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HCPCS Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C9735</td>
<td>Anoscopy; with directed submucosal injection(s), any substance</td>
</tr>
<tr>
<td>L8605</td>
<td>Injectable bulking agent, dextranomer/hyaluronic acid copolymer implant, anal canal</td>
</tr>
<tr>
<td>L8699</td>
<td>Prosthetic implant, not otherwise specified</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-9-CM Diagnosis Codes</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>787.60-787.63</td>
<td>Incontinence of feces</td>
</tr>
</tbody>
</table>


**References**


