Urinary Incontinence/ Voiding Dysfunction Treatments and Devices

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DESCRIPTION

Urinary voiding dysfunction includes urinary incontinence (UI) which is the inability to hold urine in the bladder and urinary retention which is the inability to pass urine out of the bladder. Urinary incontinence (UI) is a common condition affecting both genotypic XY and genotypic XX individuals. Many genotypic XX individuals experience UI due to pregnancy and childbirth, menopause, and the structure of the XX urinary tract. Many genotypic XY individuals experience incontinence along with prostate enlargement or after prostate surgery.

There are different types of urinary incontinence. This includes stress incontinence, urge incontinence/overactive bladder, mixed incontinence, overflow incontinence, functional incontinence, urinary retention, neurogenic bladder, and psychogenic incontinence.

There are various treatment options available, such as conservative therapy, surgical procedures, and supportive devices for the treatment of urinary incontinence which may include the below:

- **Conservative Therapies:** Include medical treatment or lifestyle changes: weight loss, dietary changes (some beverages my exacerbate symptoms, reduce consumption of alcoholic, caffeinated and carbonated beverages), bladder training, pelvic floor rehabilitation, Kegel exercises, vaginal weighted cones, biofeedback, topical vaginal estrogen, and catheterization. The American Urogynecologic Society recommends a minimum of three months conservative therapy treatment.
- **Surgical Procedures**: Include, but are not limited to, periurethral bulking agents, augmentation cystoplasty, bladder denervation or detrusor myomectomy, enterocystoplasty, bladder diversion, artificial urinary sphincter, and cystectomy. Patients whose symptoms persist despite conservative therapies for a minimum of three months should have further surgical evaluation to discuss surgical options.
- **Other measures and supportive devices for the management of urinary incontinence**: Include intermittent catheterization, indwelling urethral catheterization, suprapubic catheters, external collection systems, urethral insert devices (Attain), penile compression device, pelvic organ support devices, sling systems (MiniArc) and absorbent garments.
- **Pelvic Floor Stimulation (PFS)**: This involves the electrical stimulation of the pelvic floor muscles using a probe wired to a device controlling the electrical stimulation, or more recently, extracorporeal pulsed magnetic innervation. It is believed that electric or magnetic stimulation leads to PFS, which in turn stimulates the pudendal nerve to improve urethral closure by activating the pelvic musculature by enhancing the process of re-innervation. PFS is an off-label use for electrical stimulation devices.
- **Posterior tibial nerve stimulation (PTNS)** The procedure for PTNS consists of the insertion of a needle above the medial malleolus into the posterior tibial nerve followed by the application of low voltage (10mA, 1–10 Hz frequency) electrical stimulation that produces sensory and motor responses (i.e., a tickling sensation and plantar flexion or fanning of all toes). Noninvasive PTNS has also been delivered with surface electrodes.

Clinical Context and Therapy Purpose

In patients with urinary incontinence is to provide treatment option(s) that is an alternative to or an improvement on existing therapies.

Populations

The relevant population of interest is individuals with urinary incontinence.

Interventions

Therapies being considered:

- **Surgical Procedures**: Include, but are not limited to, periurethral bulking agents, augmentation cystoplasty, bladder denervation or detrusor myomectomy, enterocystoplasty, bladder diversion, artificial urinary sphincter, and cystectomy.

Patients whose symptoms persist despite conservative therapies for a minimum of three months should have further surgical evaluation to discuss surgical options.

- **Other measures and supportive devices for the management of urinary incontinence**: Include intermittent catheterization, indwelling urethral catheterization, suprapubic catheters, external collection systems, urethral insert devices (Attain), penile compression device, pelvic organ support devices, sling systems (MiniArc) and absorbent garments.
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Comparators

The following therapies are currently being used to make decision above urinary incontinence:

- **Conservative Therapies:** Include medical treatment or lifestyle changes: weight loss, dietary changes (some beverages my exacerbate symptoms, reduce consumption of alcoholic, caffeinated and carbonated beverages), bladder training, pelvic floor rehabilitation, Kegel exercises, vaginal weighted cones, biofeedback, topical vaginal estrogen, and catheterization. The American Urogynecologic Society recommends a minimum of three months conservative therapy treatment.

Outcomes

The general outcomes of interest are symptom reduction, symptom recurrence, and treatment-related adverse events (e.g., pain, infection). Beneficial effects may last between 3 and 12 months.

Evidence Review

Artificial Urinary Sphincter (AUS)

The artificial urinary sphincter (AUS) is an externally controlled urethral occlusion device. The transfer of fluid within the device is controlled by a pressure-regulating balloon placed extra-peritoneally in the individual's pelvis or abdominal cavity and a control pump placed in a subcutaneous pocket in the scrotum. Squeezing of the pump allows fluid within the closed-loop system to be transferred from the cuff to the balloon. It takes a few minutes before the cuff re-inflates automatically to the preset level, allowing the urethra to remain open for voiding. The valve then automatically re-tightens

several minutes later which closes the urethra, thereby enabling control of urine flow and continence to be achieved.

Potential candidates for AUS implantation should be evaluated preoperatively to exclude severe detrusor instability as well as to ensure adequate bladder stability and compliance prior to implantation of the AUS. Appropriate candidates for implantation of an AUS must have adequate motivation and sufficient manual dexterity to operate the device. Post-prostatectomy patients should wait 6 to 12 months and attempt behavioral and pharmacologic therapies first.

Several observational studies have evaluated the use of artificial urinary sphincter (AUS) in male adults with refractory urinary incontinence due to intrinsic sphincter deficiency (ISD) following prostate surgery. A multicenter retrospective cohort study was published by Tutolo et. al. (2019) which included 892 cases of AUS implantation in men with non-neurogenic stress urinary incontinence (SUI) after prostate surgery who were followed for at least 1 year. The mean length of follow-up was 32 months (range 12 to 300 months). The primary outcome was the dry rate (DR), defined as not needing to use any pads. Data on pad use prior to surgery were available for 547 of the 892 individuals in the cohort (61%). All the 547 individuals used at least 1 pad per day prior to treatment, including 368 (67%) who used at least 5 pads. At follow-up, the DR was 58% for the cohort. Among individuals without previous incontinence surgery, 409 of 724 (57%) were dry at follow-up, and the DR was 48% in individuals with previous incontinence surgery (80 of 168). The overall complication rate was 28% (248 individuals) and consisted of erosion, infection, urethral atrophy and mechanical failure.

In 2019, Boswell et. al. evaluated the long-term survival and reintervention rates. The study included 1154 individuals who underwent AUS placement for SUI following radical prostatectomy or other prostate procedure. Individuals were followed for a mean of 5.4 years. The rate of secondary surgery (removal or revision) was 35% (404 of 1154). According to Kaplan-Meier survival analysis, estimates of rates of device survival were 72% at 5 years, 56% at 10 years, 41% at 15 years and 33% at 20 years.

In a systematic review by Bomba et. al. (2019) that studied men with post-prostatectomy incontinence who were treated with artificial urinary sphincter (AUS) or an adjustable sling the authors identified seven studies with a total of 463 participants, 420 of whom had SUI following prostatectomy. In the studies, 313 received an AUS and 107 received an adjustable sling. There were no RCTs and no head-to-head comparisons of AUS and adjustable slings. The primary outcome of the review was decreased pad use. The analysis for this outcome included three studies on each intervention. Compared with no intervention, pad use decreased with either intervention and there was no statistically significant difference between interventions.

In 2017 Sacomani et. al. reported on long-term outcomes in 121 consecutive individuals who underwent artificial urinary sphincter (AUS) implantation following prostatectomy. After a mean follow-up of 5.2 years, 106 men (88%) still had their AUS device and 82 of

these (68%) reported being completely dry. Investigators have noted high complication rates, (for example, infection, erosion, mechanical failure, and device explantation) and need for reoperative procedures in up to 20% of implanted individuals. For these reasons, AUS is not considered a first-line therapy and is reserved for those who have not responded to conventional treatment options for at least 6 months following prostate surgery.

Summary of Evidence
Based on the review of peer reviewed medical literature the artificial urinary sphincter (AUS) has been shown to be effective for urinary incontinence (UI) due to intrinsic urethral sphincter deficiency (IUSD) following prostate surgery. AUS is not considered a first-line therapy and is reserved for those who have not responded to conventional treatment options for at least 6 months following prostate surgery. The evidence is sufficient to determine the technology results in improvement in net health outcomes.

The artificial urinary sphincter (AUS) may also be utilized in individuals with epispadias-exstrophy in whom bladder neck reconstruction has failed; women in whom behavioral or pharmacologic therapies, or other surgical options have failed; and children with intractable UI who are refractory to pharmacologic therapies or unsuitable for other types of operation.

Denormandie (2021) et. al., reported on an uncontrolled retrospective study on 45 women over 75 years old with stress urinary incontinence (SUI) due to intrinsic urethral sphincter deficiency (ISD) who had artificial urinary sphincter (AUS) implantation. During surgery, bladder dome injuries occurred in 9 (20%) of women and vaginal injuries occurred in 3 (6.7%) women. There were 26 early postoperative complications in 18 individuals (40%); all except 1 were minor complications. Median follow-up was 36 months. Five individuals died for reasons unrelated to the surgery and did not complete follow-up. Late postoperative complications occurred in 7 women (15.5%). At the final follow-up, 32 of the 45 individuals (71%) had their original AUS, 2 had explanted AUS, 9 had AUS revisions and 2 had AUS deactivations. In an intention-to-treat analysis, 31 of the 45 women (69%) had total continence at last follow-up.

In 2020, Barakat et. al., in a systematic review published on artificial urinary sphincter (AUS) for XX individuals with stress urinary incontinence (SUI) identified 15 uncontrolled retrospective and prospective studies with a mean of 68 individuals per study. The authors rated the quality of evidence as very low quality due to high risk of bias in all of the included studies as well as publication bias and “serious imprecision”. In a meta-analysis, the authors noted a high degree of heterogeneity in the post-operative continence rate and found a median continence rate of 79%. They also found a revision rate of 15%. Despite the high rate of post-operative continence, the authors concluded that the low quality of evidence and small study population were insufficient to draw firm conclusions about the impact of AUS on the net health outcome in XX individuals.

Summary of Evidence
To date, the evidence from well-designed studies is insufficient to form conclusions regarding the safety and efficacy of AUS for other subgroups, such as XX individuals and, children with intractable incontinence, and XY individuals who have not undergone prostate surgery. Further randomized controlled trials (RCTs) with long term follow-up are needed to determine the safety and efficacy. The evidence is insufficient to determine the effects of this technology on net health outcomes.

inFlow Intraurethral Valve-Pump and Activator
The inFlow intraurethral valve-pump and activator is a urinary device for women with incomplete bladder emptying, due to impaired detrusor contractility (IDC). The inFlow is promoted as an alternative to urinary catheters. The device consists of a small catheter with an internal magnetically activated pump-valve mechanism which is placed in the female urethra for up to 29 days or less. Upon activation by a battery-powered wand held low over the pubic area, the valve open and the pump induces urine flow. The device blocks urine flow when continence is desired, and an internal pump draws urine out of the bladder when activated by the user. Proper device sizing and initial insertion is done by a physician. Subsequent device replacements are self-inserted, or inserted by a caregiver, approximately every 29 days.

At this time, there is only a single published peer-reviewed article describing the use of the inFlow intraurethral valve-pump, which received clearance through the FDA's de novo approval process in 2014. This prospective, single-arm crossover study by Chen in 2005 involved 273 subjects with hypocontractile or acontractile bladder conditions. The first 88 subjects were enrolled directly into the study phase involving an 8-week baseline phase using clean intermittent catheterization (CIC), followed by a 16-week inFlow treatment phase, and a final 4-week treatment withdrawal phase. Subsequent subjects were first enrolled in a 1-week tolerability trial (n=185). Those subjects that satisfactorily passed that phase (n=139) continued to the study phase. A total of 196 of the original 273 (72%) subjects withdrew from the study. These withdrawals were attributed to initial discomfort and leakage of the device. A total of 77 subjects completed the inFlow treatment phase. Post-void residual volume was comparable during baseline CIC phase and inFlow treatment phase (20.3 ml versus 16.1 ml), with significantly improved quality of life ($p<0.001$). The published evidence currently available indicates that the inFlow device shows some promise for female individuals with incomplete bladder emptying, due to impaired detrusor contractility of neurologic origin, but larger more rigorous trials are needed to fully evaluate its safety and efficacy.

The evidence is insufficient to determine the effects of this technology on net health outcomes.

Laser Therapy (GeniTyte Procedure)
The GeniTyte procedure is a new treatment approach for the treatment of stress urinary incontinence. It involves the use laser that stimulates the skin's natural production of collagen making it more supple and elastic. GeniTyte works to regain bladder control by

tightening the tissue around the urethra. The number of treatments needed to restore the function of a woman's urethra supposedly depends largely on how much collage is still present in her skin. The clinical value of the GeniTyte procedure needs to be validated by well-designed studies. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Periurethral Bulking Agents

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

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

Treatment of Stress Urinary Incontinence (SUI)

Systematic Reviews

In 2021, Hoe et. al., completed a systematic review that compared the efficacy and safety of all urethral bulking agents for the treatment of women with SUI.[4,] The review included 56 articles. Since there was substantial heterogeneity of patient cohorts across studies and variability in outcomes reported, only a qualitative data analysis was performed. Overall, the authors concluded that the data support the use of Bulkamid and Macroplastique for the treatment of SUI with a short-term efficacy of 30% to 90% and 40% to 85%, respectively. Long-term efficacy for these bulking agents is 42% to 70% and 21% to 80%, respectively. Of all available bulking agents, Bulkamid appears to have the more favorable safety profile, with no cases of erosion or migration associated with its use. Of note, direct comparisons of the urethral bulking agents have not been performed.

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

In 2017, a Cochrane review by Kirchin et. al., evaluated periurethral bulking agents for urinary incontinence in women identified 14 RCTs (sample ranges, 30 to 355 patients)

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

In 2017, a joint guideline by the American Urological Association/Society of Urodynamics

Key factors in determining the optimal product are biocompatibility, durability, and absence of migration. A number of periurethral bulking agents to treat urinary incontinence have been cleared for marketing by the U.S. Food and Drug Administration (FDA); however, products developed to date have not necessarily met all criteria of the ideal bulking agents. The first FDA approved product was cross-linked collagen (e.g., Contigen). The agent was found to be absorbed over time and symptoms could recur, requiring additional injections. Contigen production was discontinued in 2011. Other periurethral bulking agents cleared by FDA for urinary incontinence include carbon-coated beads (e.g., Durasphere), spherical particles of calcium hydroxylapatite (CaHA®) in a gel carrier (Coaptite®), polydimethylsiloxane (silicone, Macroplastique®), cross-linked polyacrylamide hydrogel (Bulkamid®), and ethylene vinyl alcohol copolymer implants (e.g., Tegress®, formerly Uryx®). Tegress was voluntarily removed from the market due to safety concerns.

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. The trials vary by bulking agents used and comparator interventions (e.g., placebo, conservative therapy, surgical procedure, another bulking agent). 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 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.

Non-Food and Drug Administration Approved Bulking Agents

Dextranomer/Hyaluronic Acid (Zuidex®)

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

Polytetrafluoroethylene (Teflon)

Per review of the peer reviewed medical literature no published clinical trials were identified on polytetrafluoroethylene (Teflon) as a bulking agent.

Bulking Agents not Requiring FDA Approval

Autologous Fat and Autologous Ear Chondrocytes

Other materials have been used as bulking agents but have not demonstrated the same sustained effectiveness as cross-linked collagen or carbon-coated beads.

In a double-blind RCT of 56 women that compared periurethral injections of autologous fat (treatment group) with saline (placebo group), Lee et. al., found that periurethral fat injections were not more efficacious than placebo for treating stress incontinence. At 3 months, only 6 (22.2%) of 27 patients in the treatment group and 6 (20.7%) of 29 in the placebo group were cured or improved. In addition, 1 death occurred as a result of a pulmonary fat embolism. In another clinical trial of 32 women, Bent et. al., reported that 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 procedure.

Autologous Cellular Therapy

Strasser et. al. published the first randomized controlled trial (RCT) using autologous cell therapy to treatment stress urinary incontinence (SUI). However, Lancet retracted the publication of this trial due to ethical and quality concerns.

A phase 3 trial (NCT01382602) with 150 patients was in completed in 2017, but trial results were not identified.

Summary of Evidence
Based on review of the peer reviewed medical literature for the following bulking agents (e.g., autologous cellular therapy, autologous fat, autologous ear chondrocytes, Teflon, and Zuidex), there are few randomized controlled trials (RCTs) and little evidence of efficacy. The evidence is insufficient to determine the effects of the technology on net health outcomes.

Treatment of Vesicoureteral Reflux (VUR)
Most seen in children, vesicoureteral reflux (VUR) is the retrograde flow of urine from the bladder upward toward the kidney. The primary management strategies have been prophylactic antibiotics to reduce urinary tract infections and, for higher grade disease, surgical correction of the underlying reflux. Injection of periureteral bulking agents is proposed as an alternative to surgical intervention.

Vesicoureteral reflux (VUR) predisposes patients to urinary tract infections (UTIs) and renal infection (pyelonephritis) by facilitating the transport of bacteria from the bladder to the upper urinary tract. Pyelonephritis causes renal scarring in as many as 40% of children, and extensive scarring may lead to renal insufficiency and hypertension. The period between first renal scarring from pyelonephritis and the development of hypertension or end-stage renal disease can be 30 to 40 years.

In most cases, VUR is diagnosed after a febrile UTI episode or abnormality seen on ultrasound imaging. Approximately one-third of children with UTIs are found to have VUR. The average age for UTI onset is 2 to 3 years, corresponding to the age when toilet training occurs. The criterion standard for diagnosis is voiding cystourethrography, a procedure that involves catheterization of the bladder. Voiding cystourethrography is indicated if renal and bladder ultrasonography reveals hydronephrosis, scarring, or other findings that would suggest either high-grade VUR or obstructive uropathy, as well as in other atypical or complex clinical circumstances. The severity of reflux is described by a grade, typically with the International Reflux Study Group grading system, which grades severity from I (reflux partway up the ureter) to V (massive reflux of urine up the ureter with marked tortuosity and dilation of the ureter and calyces).

Treatment strategies for VUR include bladder training, antibiotic prophylaxis, and surgical modification of the ureter to correct the underlying reflux. Open surgical treatment is typically reserved for patients with high-grade reflux (grades III and IV) or as salvage therapy for those who are noncompliant with antibiotic therapy or have breakthrough UTIs while receiving prophylactic therapy. Surgical management involves lengthening the intramural ureter by modification of the ureterovesical attachment with reimplantation of the ureter.

Treatment of VUR remains controversial. There is a lack of good evidence that VUR actually increases the risk of pyelonephritis and renal scarring, and the long period of time before renal scarring, hypertension, and end-stage renal disease makes these serious conditions difficult to study. Moreover, VUR has a relatively high rate of spontaneous

resolution (>60% over 5 years), so many children may not benefit from treatment. An important challenge is to identify the subset of children most likely to benefit from VUR treatment. At present, in the absence of definitive answers on the utility of treating VUR or the best treatment option, antibiotic prophylaxis to prevent recurrent UTIs and surgery to treat the underlying reflux remain accepted management strategies.

The use of bulking agents in the treatment of VUR has been reported for more than 20 years and suggested as an alternative to antibiotic and surgical therapy. Bulking agents can be injected into tissue around the ureteral orifices to minimize reflux. The STING procedure (subureteral transurethral injection) involves the endoscopic injection of a bulking agent into the submucosal bladder wall just below the ureteral opening. In the modified STING procedure, the needle is placed in the ureteral tunnel, and the bulking agent is injected into the submucosal intraureteral space. When successfully injected, the compound tracks along the length of the detrusor tunnel and establishes a coapted ureteral tunnel. More recently, the HIT (hydrodistension of the ureteric orifice and injection of bulking agents in the mid to distal submucosal tunnel at the 6 o'clock position) and double HIT (modified HIT with proximal and distal intraluminal submucosal injections) techniques have gained favor; a meta-analysis revealed that overall VUR resolution was 82.5% with HIT as compared to 71.4% with STING ($p<0.00001$). These endoscopic procedures can be performed in an outpatient setting.

A variety of bulking agents have been tested for biocompatibility and absence of migration, in 2001, Deflux (dextranomer/hyaluronic acid copolymer) was approved by the U.S. Food and Drug Administration (FDA) for the "treatment of children with vesicoureteral reflux (VUR) grades II-IV" and remains the only FDA approved bulking agent for VUR.

Summary Evidence
For children who have VUR who have failed medical therapy and are eligible for surgery who receive endoscopic treatment with periureteral bulking agents, the evidence includes randomized controlled trials and systematic reviews. Overall, studies have reported similar rates of reflux resolution compared with ureteral reimplantation surgery and the body of evidence would suggest that morbidity rates are similar or lower with bulking agents. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For children who have VUR who have not failed medical therapy and may be ineligible for surgery who receive endoscopic treatment with periureteral bulking agents, the evidence includes randomized controlled trials. The randomized controlled trials, which had relatively small sample sizes in each arm, compared periureteral bulking agents with antibiotic prophylaxis and/or surveillance only and reported mixed findings. Additional, larger studies are needed before conclusions can be drawn about the efficacy of periureteral bulking agents as first-line treatment for patients with VUR. The evidence is insufficient to determine the effects of the technology on health outcomes.

Pelvic Floor Stimulation
Pelvic floor stimulation (PFS) is proposed as a nonsurgical treatment option for individuals with urinary incontinence. This approach involves either electrical stimulation of pelvic floor musculature or extracorporeal pulsed magnetic stimulation.

Pelvic floor stimulation (PFS) involves electrical stimulation of pelvic floor muscles using either a probe wired to a device for controlling the electrical stimulation or, more recently, extracorporeal electromagnetic (also called magnetic) pulses. Stimulation of the pudendal nerve to activate the pelvic floor musculature may improve urethral closure. In addition, PFS is thought to improve partially denervated urethral and pelvic floor musculature by enhancing the process of reinnervation. Methods of electrical PFS have varied in location (e.g., vaginal, rectal), stimulus frequency, stimulus intensity or amplitude, pulse duration, pulse to rest ratio, treatments per day, number of treatment days per week, length of time for each treatment session, and overall time period for device use between clinical and home settings. Variations in the amplitude and frequency of the electrical pulse are used to mimic and stimulate the different physiologic mechanisms of the voiding response, depending on the etiology of the incontinence (ie, either detrusor instability, stress incontinence, or a mixed pattern). Magnetic PFS does not require an internal electrode; instead, patients sit fully clothed on a specialized chair with an embedded magnet.

Patients receiving electrical PFS may undergo treatment in a physician's office or physical therapy facility, or patients may undergo initial training in a physician's office followed by home treatment with a rented or purchased pelvic floor stimulator. Magnetic PFS may be administered in the physician's office

Electrical Pelvic Floor Stimulation (PFS)
Based on review of the peer reviewed medical literature most of the randomized controlled trials (RCTs) on electrical pelvic floor stimulation (PFS) for urinary incontinence have been published prior to 2001. Systematic review and meta-analyses of RCTs have had inconsistent findings on the impact of this treatment compared to sham treatment related to urinary incontinence.

Randomized controlled trials (RCTs) have evaluated electrical pelvic floor stimulation (PFS) as a treatment of postprostatectomy urinary incontinence. Some of these studies reported improvements in some outcomes but have limitation such as failure to isolate the effect of electrical PFS; and/or failure to find a sham comparator or an accepted treatment comparator. Pooled analyses from 3 systematic reviews found inconsistent evidence on the effect of PFS on continence at 3 months (1 found significant benefit and 2 did not) and found no clear benefit of PFS at 6- and 12-month follow-up.

Magnetic Pelvic Floor Stimulation
A systematic review of randomized controlled trials (RCTs) published on magnetic pelvic floor stimulation (PFS) for the treatment of urinary incontinence in women identified 8 blinded, sham-controlled trials (N=484 patients). Treatment protocols

(e.g., frequency, duration of magnetic PFS) varied among trials. The primary outcome was cure rate; only 1 trial reported this outcome, so data were not pooled. A meta-analysis of 3 studies reporting improvements in the continence rates found significantly greater improvement in the treatment group than in the sham group (RR, 2.29; 95% CI, 1.60 to 3.29). Due to the variability across trials in types of incontinence treated and/or outcome reporting, data were not pooled for other outcomes. Reviewers noted that the evidence was limited by low-quality trials with short-term follow-up.

A randomized controlled trial (RCT) was identified on magnetic pelvic floor stimulation (PFS) for the treatment of postprostatectomy urinary incontinence. There was a greater improvement in pad weight at 2 months in the magnetic PFS group than in the pelvic floor muscle exercises group but there were no significant differences between groups beginning at 3 months. Other outcomes also did not favor the magnetic PFS group.

Summary of Evidence
For individuals who have urinary incontinence who receive electrical pelvic floor stimulation (PFS), the evidence includes systematic reviews of randomized controlled trials (RCTs). Findings from systematic reviews have not found that electrical PFS used to treat urinary incontinence in XX individuals consistently improves the net health outcome compared with placebo or other conservative treatments. Moreover, meta-analyses of RCTs have not found a significant benefit of electrical PFS in XY individuals with postprostatectomy incontinence compared with a control intervention. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have urinary incontinence who receive magnetic elvic floor stimulation (PFS), the evidence includes randomized controlled trials (RCTs) and a systematic review. A systematic review of RCTs on magnetic PFS for urinary incontinence in XX individuals concluded that the evidence was insufficient due to the following factors: a low number of trials with short-term follow-up, methodologic limitations, as well as heterogeneity in patient populations, interventions, and outcomes reported. One RCT evaluating magnetic stimulation for treating XY individuals with postprostatectomy urinary incontinence reported short-term results favoring magnetic PFS; however, the trial was small and lacked a sham comparator. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Posterior Tibial Nerve Stimulation
Posterior Tibial Nerve Stimulation (PTNS) (also known as percutaneous tibial nerve stimulation) is an electrical neuromodulation technique used primarily for treatment voiding dysfunction.

Posterior Tibial Nerve Stimulation (PTNS) has also been proposed as a treatment for non-neurogenic and neurogenic bladder syndromes

Voiding Dysfunction
Common causes of non-neurogenic voiding dysfunction are pelvic floor neuromuscular changes (e.g., from pregnancy, childbirth, surgery), inflammation, medication (e.g., diuretics, anticholinergics), obesity, and psychogenic factors. Overactive bladder is a non-neurogenic voiding dysfunction characterized by urinary frequency, urgency, urge incontinence, and nonobstructive retention.

Neurogenic bladder dysfunction is caused by neurologic damage in patients with multiple sclerosis, spinal cord injury, detrusor hyperreflexia, or diabetes with peripheral nerve involvement. The symptoms include overflow incontinence, frequency, urgency, urge incontinence, and retention.

Approaches to the treatment of incontinence differentiate between urge incontinence and stress incontinence. Conservative behavioral management such as lifestyle modification (e.g., dietary changes, weight reduction, fluid management, smoking cessation) along with pelvic floor exercises and bladder training are part of the initial treatment of overactive bladder symptoms and both types of incontinence. Pharmacotherapy is another option, and different medications target different symptoms. Some individuals experience mixed incontinence.

If conservative behavioral therapies and pharmacotherapy are unsuccessful, percutaneous tibial nerve stimulation (PTNS) may be recommended.

The current indication cleared by the U.S. Food and Drug Administration (FDA) for PTNS is overactive bladder and associated symptoms of urinary frequency, urinary urgency, and urge incontinence.

Altering the function of the posterior tibial nerve with PTNS is believed to improve voiding function and control. The mechanism of action is believed to be retrograde stimulation of the lumbosacral nerves (L4-S3) via the posterior tibial nerve located near the ankle. The lumbosacral nerves control the bladder detrusor and perineal floor.

Administration of PTNS consists of inserting a needle above the medial malleolus into the posterior tibial nerve followed by the application of low-voltage (10 mA, 1-10 Hz frequency) electrical stimulation that produces sensory and motor responses as evidenced by a tickling sensation and plantarflexion or fanning of all toes. The recommended course of treatment is an initial series of 12 weekly office-based treatments followed by an individualized maintenance treatment schedule.

For individuals who have non-neurogenic urinary dysfunction including overactive bladder (OAB) who have failed behavioral and pharmacologic therapy and received an initial course of PTNS, several RCTs of PTNS have been published, including 2 key industry sponsored RCTs, the OrBIT and SUmiT trials. Systematic reviews of the evidence have found short-term improvements with PTNS. The largest, highest quality study was the blinded, sham controlled SUmiT trial. This trial reported a statistically

significant benefit of PTNS versus sham at 12 weeks. In another small sham-controlled trial, a 50% reduction in urge incontinent episodes was attained in 71% of the PTNS group compared with 0% in the sham group. The nonblinded OrBIT trial found that PTNS was noninferior to medication treatment at 12 weeks.

For individuals who have OAB syndrome who have failed behavioral and pharmacologic therapy, respond to an initial course of PTNS, and then receive maintenance PTNS therapy, there are up to 36 months of observational data that suggest there is a durable effect for some of these patients. The SUmiT and OrBIT trials each included extension studies, which followed individuals who responded to the initial course of PTNS and continued to receive periodic maintenance therapy. There is variability in the interval between and frequency of maintenance treatments, and an optimal maintenance regimen remains unclear. While comparative data are not available after the initial 12-week treatment period, the observational data support a clinically meaningful benefit for use in individuals who have already failed behavioral and pharmacologic therapy and respond to the initial course of PTNS. Percutaneous tibial nerve stimulation may allow such individuals to avoid more invasive interventions. Adverse events appear to be limited to local irritation for both short- and long-term PTNS use. Typical regimens schedule maintenance treatments every 4-6 weeks.

Few randomized controlled trials (RCTs) evaluating posterior tibial nerve stimulation for treating neurogenic bladder have been published to date. Studies varied widely in study populations and comparator interventions. Study findings have not suggested that tibial nerve stimulation significantly reduces incontinence symptoms and improves other outcomes.

Summary of Evidence
For individuals who have non-neurogenic urinary dysfunction including overactive bladder (OAB) and have failed conservative behavioral and pharmacologic therapy who receive an initial course of posterior tibial nerve stimulation (PTNS), the evidence includes randomized sham-controlled trials, randomized controlled trials (RCTs) with an active comparator, and systematic reviews. The SUmiT and OrBIT trials are 2 key industry-sponsored RCTs. Systematic reviews that included these and other published trials have found short-term reductions in voiding dysfunction with PTNS. The largest, highest quality study was the double-blind, sham-controlled SUmiT trial, which reported a statistically significant benefit of PTNS versus sham at 12 weeks. In an additional, small sham-controlled trial, a 50% reduction in urge incontinent episodes was attained in 71% of the PTNS group compared with 0% in the sham group. The nonblinded OrBIT trial found that PTNS was noninferior to medication therapy at 12 weeks. Adverse events were limited to local irritation effects. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have overactive bladder (OAB) syndrome that has failed conservative behavioral and pharmacologic therapy who respond to an initial course of posterior tibial nerve stimulation (PTNS) who receive maintenance PTNS, the evidence

includes observational studies and systematic reviews. The SUmiT and OrBIT trials each included extension studies that followed individuals who responded to the initial course of PTNS and continued to receive periodic maintenance therapy. There is variability in the interval between and frequency of maintenance treatments, and an optimal maintenance regimen remains unclear. There are up to 36 months of observational data available, reporting that there is a durable effect for some of these patients. While comparative data are not available after the initial 12-week treatment period, the observational data support a clinically meaningful benefit for use in individuals who have already failed behavioral and pharmacologic therapy and who respond to the initial course of PTNS. Percutaneous tibial nerve stimulation may allow such individuals to avoid more invasive interventions. Adverse events appear to be limited to local irritation for both short- and long-term PTNS use. Typical regimens schedule maintenance treatments every 4-6 weeks. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have neurogenic bladder dysfunction who receive posterior tibial nerve stimulation (PTNS), the evidence includes several randomized controlled trials (RCTs) and a systematic review of RCTs and observational data. Only a few RCTs evaluating posterior tibial nerve stimulation for treating neurogenic bladder have been published to date, and studies varied widely in factors such as study populations and comparator interventions. Study findings have not reported that PTNS significantly reduced incontinence symptoms and improved other outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

ProACT Adjustable Continence Therapy

The ProACT adjustable continence system consists of two postoperatively adjustable silicone balloons placed under fluoroscopic guidance at the prostatic apex (in post-TURP individuals), or at the vesico-urethral anastomosis (in post prostatectomy subjects) in males. Balloon titration is via tubing connected to a titanium port in the scrotum to enable post-implantation adjustments. The balloons are filled with isotonic solution following implantation; 1 ml can be titrated monthly until optimum continence is achieved.

FDA clearance was based on results of a prospective, multi-center, single-arm, open-label clinical study of 123 subjects in the intent-to-treat cohort. Subjects were followed for a minimum of 18 months following implantation with continued follow-up planned. The primary effectiveness endpoint was the average of two 24-hour pad weight measurements conducted at baseline compared to the average of two 24-hour pad weight measurements conducted at 18 months. Individual success was defined as ≥ 50% reduction in 24-hour pad weight at 18 months, compared to baseline. Overall study success criteria was defined as an exact 95% binomial confidence interval lower boundary of ≥ 50% success at 18 months. The success rate, which was based on the primary endpoint, was 46% (57/124) (95% CI, 37% to 55%), which did not meet the performance goal because the lower bound of the 95% CI was 37%, which is below the target responder rate of 50%. It was concluded that the study's primary effectiveness endpoint was not met.

Several additional single-arm studies evaluating ProAct in men with SUI following prostate surgery have been published (Nestler, 2018; Noorhoff 2017, Ronzi, 2019). Complication rates and/or need for revision surgery tended to be high. In the Nestler (2018) study, 59 of 112 implants of the ProAct system (53%) had to be revised after a median of 26 months due to rupture or dislocation/migration. Ronzi and colleagues (2019) identified complications in 70 of 102 cases (69%) including 34 migrations, 18 device failures, 28 urethral erosions and 28 cutaneous erosions.

A systematic review of studies on ProAct in men with SUI was published in 2019 by Larson and colleagues. No RCTs were identified. The authors included 19 studies with a total of 1264 individuals. In a pooled analysis of data on ProAct treatment, 60.2% of individuals were 'dry' at follow-up and 81.9% were either 'dry' or 'improved'. No data from any comparison intervention were reported. A pooled analysis of adverse event data from 18 studies found a 5.3% rate of intraoperative bladder or urethra perforation and a 22.2% revision rate over a mean follow-up of 3.6 years.

The evidence is insufficient to determine the effects of this technology on net health outcomes.

Tactile Biomechanical Sensor Imaging
The Kegel perineometer or vaginal manometer was developed as an instrument **to** measure the strength of voluntary contractions of the pelvic floor muscles. Using the perineometer ascertains the air pressure inside the vagina when asking the woman to squeeze as hard as possible, which indicates whether doing Kegel exercises would be beneficial. Assessment of the pelvic floor strength can also be performed digitally by the physician during a gynecological exam digitally to identify women with fascial defects of the pelvic floor. The Kegel perineometer and digital examinations are said to identify those women at risk of genital prolapse or urinary incontinence. Based on review of the peer reviewed medical literature additional studies are needed to evaluate the applications, strengths, and limitations of this type of tactile imaging for diagnostic use. There are currently no professional guidelines and position statements that support the use of vaginal tactile imaging or biomechanical tactile sensor imaging for any gynecological or non-gynecological condition.

The evidence is insufficient to determine the effects of this technology on net health outcomes.

Transvaginal and Transurethral Radiofrequency Energy
The Lyrette Transurethral SUI System: Previously known as Renessa Procedure, this procedure involves passing a specially designed 4-needle radiofrequency probe through the urethral opening into the urethra and then into the bladder. Once the probe is in position, a small balloon is inflated to keep it stationary during the procedure. Radiofrequency energy is then delivered for 60 seconds to the 4 needles, which are deployed from the probe into the tissue of the bladder neck and upper urethra. Tissue temperatures of 65 to 75 degrees Celsius are generated; at this temperature, focal

microscopic denaturation of collagen occurs. The procedure is repeated 9 times so that collagen is denatured at 36 tissue sites.

The transvaginal radiofrequency bladder neck suspension SURx Transvaginal System involves making an incision through the vagina lateral to the urethra, exposing the endopelvic fascia. Radiofrequency energy is then applied over the endopelvic fascia in a slow sweeping manner, resulting in blanching and shrinkage of the tissue.

Based on review of the peer reviewed medical literature the evidence from well-conducted, randomized, controlled trials on transvaginal and transurethral radiofrequency tissue remodeling for urinary stress incontinence remains limited in quantity and quality. It is not known whether either of these treatments leads to long-term improvements in net health outcomes compared with a sham procedure or another treatment for stress urinary incontinence; therefore, both transvaginal and transurethral radiofrequency tissue remodeling for urinary stress incontinence is considered investigational.

The evidence is insufficient to determine the effects of this technology on net health outcomes.

Vaginal Weight Training

Vaginal weight training is a behavioral therapy that employs weights during Kegel or pelvic floor exercises to strengthen pelvic floor muscles. The use of vaginal weights (cones) has not been shown to improve pelvic floor muscle strength more than Kegel exercises alone.

A systematic review completed by Cochran identified 23 randomized controlled trials (RCTs) comparing weighted vaginal cones to a control condition in women with urinary incontinence. The authors noted that all the studies had small sample sizes, some had high drop-out rates and study quality was difficult to assess in many cases. Most studies used a similar protocol in which individuals held the cones in place twice a day for 15 minutes. Outcome measures varied widely. A comparison of interest is the efficacy of vaginal cones plus pelvic floor muscle training (PFMT) alone. Two trials addressed this comparison and neither found a significant benefit of the addition of vaginal cones. Thirteen trials compared vaginal cones and PFMT. In a pooled analysis of 4 trials, there was not a significant difference between groups in leakage episodes per day (mean difference [MD], 0.00; 95% CI, -0.20 to 0.20). Similarly, a pooled analysis of 5 trials did not find a significant difference between groups in the proportion of individuals with improvement on the pad test (risk ratio [RR], 1.10; 95% CI, 0.82 to 1.49). Four trials reported on subjective improvement of cure and this outcome significantly favored the vaginal cone group (RR, 1.01; 95% CI, 0.75 to 1.36). The ability to conduct pooled analyses was limited by variability in control interventions and outcome measures and thus a relatively small number of studies were included in the meta-analyses. In these meta-analyses, objective measures did not find a significant benefit of vaginal cones compared with PFMT.

In a small prospective study that evaluated vaginal cone therapy in a passive phase (without voluntary contractions of the pelvic floor) and an active phase (with voluntary contractions). Twenty-four women with SUI were treated and 21 women completed the 3-month study. Outcomes in the pad test favored the active phase as did pelvic floor evaluation and bladder neck mobility. Complete reversal of symptomatology was observed in 12 (57.1%) participants, and satisfaction was expressed by 19 (90.4%). This study lacked a comparison group of women who did pelvic floor exercises without the use of vaginal cones.

Summary of Evidence
Based on the review of the peer reviewed medical literature which includes randomized controlled trials (RCTs) and systematic reviews studies had small sample sizes, some had high drop-out rates and study quality was difficult to assess in many cases. objective measures did not find a significant benefit of vaginal cones compared other therapies such as pelvic floor muscle training (PFMT). Further RCTs are needed. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Practice Guidelines and Position Statements

American College of Obstetricians and Gynecologists
In 2016, the American College of Obstetricians and Gynecologists issued an updated practice bulletin on urinary incontinence in women. The practice bulletin states 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.

The American Urological Society
In 2019, the American Urological Society and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction published guidelines on the diagnosis and treatment of non-neurogenic overactive bladder (OAB) in adults that included the following recommendations:

Guideline Statements

Diagnosis
1. The clinician should engage in a diagnostic process to document symptoms and signs that characterize OAB and exclude other disorders that could be the cause of the patient's symptoms; the minimum requirements for this process are a careful history, physical exam, and urinalysis. *Clinical Principle*

2. In some patients, additional procedures and measures may be necessary to validate an OAB diagnosis, exclude other disorders and fully inform the treatment plan. At the clinician's discretion, a urine culture and/or post-void residual assessment may be performed and information from bladder diaries and/or symptom questionnaires may be obtained. *Clinical Principle*
3. Urodynamics, cystoscopy and diagnostic renal and bladder ultrasound should not be used in the initial workup of the uncomplicated patient. *Clinical Principle*
4. OAB is not a disease; it is a symptom complex that generally is not a life-threatening condition. After assessment has been performed to exclude conditions requiring treatment and counseling, no treatment is an acceptable choice made by some patients and caregivers. *Expert Opinion*
5. Clinicians should provide education to patients regarding normal lower urinary tract function, what is known about OAB, the benefits versus risks/burdens of the available treatment alternatives and the fact that acceptable symptom control may require trials of multiple therapeutic options before it is achieved. *Clinical Principle*

Treatment:

First-Line Treatments: Behavioral Therapies

6. Clinicians should offer behavioral therapies (e.g., bladder training, bladder control strategies, pelvic floor muscle training, fluid management) as first line therapy to all patients with OAB. *Standard (Evidence Strength Grade B)*
7. Behavioral therapies may be combined with pharmacologic management. *Recommendation (Evidence Strength Grade C)*

Second-Line Treatments: Pharmacologic Management

8. Clinicians should offer oral anti-muscarinics or oral β_3-adrenoceptor agonists as second-line therapy. *Standard (Evidence Strength Grade B)*
9. If an immediate release (IR) and an extended release (ER) formulation are available, then ER formulations should preferentially be prescribed over IR formulations because of lower rates of dry mouth. *Standard (Evidence Strength Grade B)*
10. Transdermal (TDS) oxybutynin (patch or gel) may be offered. *Recommendation (Evidence Strength Grade C)*
11. If a patient experiences inadequate symptom control and/or unacceptable adverse drug events with one anti-muscarinic medication, then a dose modification or a different anti-muscarinic medication or a β_3-adrenoceptor agonist may be tried. *Clinical Principle*
12. Clinicians may consider combination therapy with an anti-muscarinic and β_3-adrenoceptor agonist for patient's refractory to monotherapy with either anti-muscarinics or β_3-adrenoceptor agonists. *Option (Evidence Strength Grade B)*
13. Clinicians should not use anti-muscarinics in patients with narrow-angle glaucoma unless approved by the treating ophthalmologist and should use anti-muscarinics with extreme caution in patients with impaired gastric emptying or a history of urinary retention. *Clinical Principle*

14. Clinicians should manage constipation and dry mouth before abandoning effective anti-muscarinic therapy. Management may include bowel management, fluid management, dose modification or alternative anti-muscarinics. *Clinical Principle*
15. Clinicians must use caution in prescribing anti-muscarinics in patients who are using other medications with anti-cholinergic properties. *Expert Opinion*
16. Clinicians should use caution in prescribing anti-muscarinics or β_3-adrenoceptor agonists in the frail OAB patient. *Clinical Principle*
17. Patients who are refractory to behavioral and pharmacologic therapy should be evaluated by an appropriate specialist if they desire additional therapy. *Expert Opinion*

Third-Line Treatments: PTNS and Neuromodulation

18. Clinicians may offer intradetrusor onabotulinumtoxinA (100U) as third-line treatment in the carefully selected and thoroughly counseled patient who has been refractory to first- and second line OAB treatments. The patient must be able and willing to return for frequent post-void residual evaluation and able and willing to perform self-catheterization if necessary. *Standard (Evidence Strength Grade B)*
19. Clinicians may offer peripheral tibial nerve stimulation (PTNS) as third-line treatment in a carefully selected patient population. *Recommendation (Evidence Strength Grade C)*
20. Clinicians may offer sacral neuromodulation (SNS) as third-line treatment in a carefully selected patient population characterized by severe refractory OAB symptoms or patients who are not candidates for second-line therapy and are willing to undergo a surgical procedure. *Recommendation (Evidence Strength Grade C)*
21. Practitioners and patients should persist with new treatments for an adequate trial in order to determine whether the therapy is efficacious and tolerable. Combination therapeutic approaches should be assembled methodically, with the addition of new therapies occurring only when the relative efficacy of the preceding therapy is known. Therapies that do not demonstrate efficacy after an adequate trial should be ceased. *Expert Opinion*

Fourth-Line Treatments: Augmentation Cystoplasty and Urinary Diversion

22. In rare cases, augmentation cystoplasty or urinary diversion for severe, refractory, complicated OAB patients may be considered. *Expert Opinion*

Additional Treatments:

23. Indwelling catheters (including transurethral, suprapubic, etc.) are not recommended as a management strategy for OAB because of the adverse risk/benefit balance except as a last resort in selected patients. *Expert Opinion*

European Urology Association and European Urogynecological Association

In 2017, the European Urology Association and European Urogynecological Association issued a joint consensus review of data on implanted material for pelvic organ prolapse and stress urinary incontinence. They stated: "Urethral balloons and injectables are not recommended as first-line therapy for SUI. Bulking agents are associated with lower cure rates of SUI when compared with colosuspension or autologous fascial slings

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

European Association of Urology
In 2018, the European Association of Urology conducted a review of therapies for urinary incontinence that included the following recommendations:

- They found that botulinum toxin, PTNS, and sacral nerve stimulation may be effective treatments for OAB. There was no high-quality evidence showing the superiority of one therapy over another. Age, comorbidities, patient preference, and surgical expertise were factors to be considered when treatment decisions are made.
- "Do not offer electrical stimulation with surface electrodes (skin, vaginal, anal) alone for the treatment of stress urinary incontinence." (Strong recommendation)
- "Do not offer magnetic stimulation for the treatment of urinary incontinence or overactive bladder in women." (Strong recommendation)

Regulatory Status

Percutaneous Tibial Nerve Stimulators
In 2005, the Urgent® PC Neuromodulation System was the initial PTNS device cleared for marketing by FDA through the 510(k) process to treat patients suffering from urinary urgency, urinary frequency, and urge incontinence. Additional percutaneous tibial nerve stimulators have been cleared for marketing through the 510(k) process. They are listed in Table 1.

The Urgent® PC Neuromodulation System and NURO™ Neuromodulation System are not FDA cleared for other indications, such as the treatment of fecal incontinence.

Wireless technology is evolving for the treatment of overactive bladder; it is approved in Europe. BlueWind (BlueWind Medical) is a wireless, battery-less, miniature implantable neurostimulator activated by an external device worn at the ankle.

Table 1. FDA-Cleared Percutaneous Tibial Nerve Stimulators (FDA Product Code: NAM)

Device Name	Manufacturer	Cleared	Indications
Urgent® PC Neuromodulation System	Uroplasty, now Cogentix Medical	Oct 2005	Treatment of urinary urgency, urinary frequency, and urge incontinence
Urgent® PC Neuromodulation System	Uroplasty, now Cogentix Medical	Jul 2006	FDA determined the 70% isopropyl alcohol prep pad contained in the kit is subject to regulation as a drug
Urgent® PC Neuromodulation System	Uroplasty, now Cogentix Medical	Aug 2007	Labeling update, intended use is unchanged
Urgent® PC Neuromodulation System	Uroplasty, now Cogentix Medical	Oct 2010	Intended use statement adds the diagnosis of overactive bladder
NURO™ Neuromodulation System	Advanced Uro-Solutions, now Medtronic	Nov 2013	Treatment of patients with overactive bladder and associated symptoms of urinary urgency, urinary frequency, and urge incontinence

Periurethral Bulking Agents

Several periurethral bulking agents have been approved by FDA through the premarket approval process and products include:

- In 1999, Durasphere (Advanced UroScience), a pyrolytic carbon-coated zirconium oxide sphere was approved for treatment of adult women with stress-type urinary incontinence caused by intrinsic sphincter insufficiency (ISD).
- In 2001 Deflux (dextranomer/hyaluronic acid) was approved for use in children with reflux grades II-IV.

- In 2004, Uryx (CR Bard) a vinyl alcohol copolymer implant was approved for the treatment of adult women diagnosed with stress urinary incontinence due to intrinsic sphincter deficiency (ISD).
- In 2005, Coaptite (Merz Aesthetics, previously BioForm Medical) spherical particles of calcium hydroxylapatite, suspended in a gel carrier was approved for the treatment of stress urinary incontinence (ISD) due to intrinsic sphincteric deficiency in adult women.
- In 2006, Macroplastique (Cogentix Medical), polydimethylsiloxane was approved in the treatment of adult women diagnosed with stress urinary incontinence primary due to intrinsic sphincter deficiency (ISD).
- In 2020, Bulkamid (polyacrylamide hydrogel) (Axonics Modulation Technologies, Inc) was approved for the treatment of stress urinary incontinence (SUI) due to intrinsic sphincter deficiency (ISD) in adult women who have SUI or stress predominant mixed incontinence.

Other Devices
In 2002, the SURx Transvaginal System received marketing clearance through the U.S. Food and Drug Administration (FDA) 510(k) process. According to the FDA, the device "is indicated for shrinkage and stabilization of female pelvic tissue for treatment of Type II stress urinary incontinence due to hypermobility in women not eligible for major corrective surgery." As of 2006, the SURx is no longer marketed in the U.S.

In 2005, Novasys Medical received clearance to market the Renessa® transurethral radiofrequency system through the FDA 510(k) process. The device is indicated for the transurethral treatment of stress urinary incontinence due to hypermobility. In 2013, Verathon acquired Renessa® by Novasys Medical®, and rebranded it as the Lyrette™.

The inFlow device obtained FDA clearance through the de novo approval process in 2014 and is indicated for, "Use in female individuals 18 years of age or older who have incomplete bladder emptying, due to impaired detrusor contractility of neurologic origin, and who are capable of operating it in accordance with instructions or who have trained caregivers"

The ProACT was approved by the FDA in November 2015 via a premarket approval (PMA) application for treatment of men with stress incontinence of at least 12 months' duration following prostate surgery who did not respond to conservative therapy.

Pelvic Floor Stimulation Devices
In 2000, the NeoControl® Pelvic Floor Therapy System (Neotonus) cleared through the FDA 510(k) process for treating urinary incontinence in women. This device, formerly known as the Neotonus Model 1000 Magnetic Stimulator, provides noninvasive electromagnetic stimulation of pelvic floor musculature. The magnetic system is embedded in a chair seat; patients sit on the chair fully clothed and receive the treatment. The magnetic fields are controlled by a separate power unit.

Several electrical stimulators have been cleared by the U.S. Food and Drug Administration (FDA). In 2006, the MyoTrac Infiniti™ (Thought Technology) and in 2015, the ApexM (InControl Medical), nonimplanted electrical stimulators for treating urinary incontinence, were cleared for marketing by the FDA through the 510(k) process. Predicate devices also used to treat urinary incontinence, including the Pathway™ CTS 2000 (Prometheus Group) and the InCare® PRS (Hollister). In 2011, the itouch Sure Pelvic Floor Exerciser (TensCare) was cleared for marketing. This product is being marketed in the United States as EmbaGYN® (Everett Laboratories).

In 2014, the InTone® MV (InControl Medical), a nonimplantable device that provides electrical stimulation and/or biofeedback via manometry, was cleared by the FDA. The device is intended to treat male and female urinary and fecal incontinence.

PRIOR APPROVAL

Not applicable.

POLICY

See Related Medical Policies

- 02.01.04 Biofeedback
- 02.01.51 Fecal Incontinence Management
- 08.01.21 Sacral Nerve Stimulation/Neuromodulation

Periurethral Bulking Agents for the Treatment of Stress Urinary Incontinence (L8603, L8606 and 51715)
The following periurethral bulking agents may be considered **medically necessary** to treat stress urinary incontinence (SUI) for individuals who are unresponsive to conservative therapy* for at least 3 months:

- Durasphere (carbon-coated spheres)
- Coaptite (calcium hydroxylapatite)
- Macroplastique (Polydimehylsiloxan)
- Crossed-link collagen bulking agents
- Bulkamid (polyacrylamide hydrogel)
- Uryx (ethylene vinyl alcohol copolymer)

*Conservative therapy for stress urinary incontinence may include:

- Pelvic floor muscle exercises (Kegel exercises)/supervised pelvic floor therapy
- Behavioral changes, such as:
    - Fluid management
    - Smoking cessation
    - Weight loss

    - Moderation of physical activities that provoke stress urinary incontinence
- Intravaginal estrogen therapy
- Use of pessary
- Treatment of other underlying causes of stress incontinence in patients amendable to these treatments

Individuals with stress urinary incontinence (SUI) and do not improve with 5 injection procedures (5 separate treatment sessions) are considered treatment failures, and any further treatment of stress urinary incontinence (SUI) with a periurethral bulking agent(s) is considered **not medically necessary**. Individuals who have a recurrence of stress urinary incontinence (SUI) following successful treatment (5 separate treatment sessions) with a periurethral bulking agent above in the past (e.g., 6-12 months previously) may benefit from additional treatment sessions. Coverage of additional sessions may be allowed but must be supported by medical documentation (e.g., documentation must be provided regarding the individual's response from prior treatment[s]).

Individuals not meeting the criteria above for the use of periurethral bulking agents for the treatment of stress urinary incontinence (SUI) is considered **not medically necessary.**

The use of any other periurethral bulking agents including but not limited to the following as a treatment for stress urinary incontinence (SUI) and any other types of urinary incontinence is considered **investigational** due to the lack of clinical evidence demonstrating an impact on improved net health outcomes:

- Autologous cellular therapy (e.g., myoblasts, fibroblasts, muscle-derived stem cells, adipose derived stem cells), autologous fat or autologous ear chondrocytes
- Dextranomer/hyaluronic acid (Zuidex® with an injection system (Implacer®; Q-Med AB)
- Polytetrafluoroethylene (Teflon)

Periurethral Bulking Agents for the Treatment of Vesicoureteral Reflux (L8604 and 52327)

Periurethral bulking agent Deflux (dextranomer/hyaluronic acid) may be considered **medically necessary** as a treatment of children (21 years and less) with vesicoureteral reflux **(**VUR) grades II, III, or IV* when medical therapy has failed, and is eligible for surgical intervention.

The use of periurethral bulking agent Deflux (dextranomer/hyaluronic acid) is considered **investigational** for all other indications due to the lack of clinical evidence demonstrating an impact on improved net health outcomes.

*The International Reflux Grading system classifies vesicoureteral reflux VUR into 5 grades, depending on the degree of retrograde filling and dilation of the renal collecting system. This system is based on the radiographic appearance of the renal pelvis and calyces on a voiding cystogram, as follows:

- Grade I: Urine backs up into the ureter only, and the renal pelvis appears healthy, with sharp calyces.
- Grade II: Urine backs up into the ureter, renal pelvis, and calyces. The renal pelvis appears healthy and has sharp calyces.
- Grade III: Urine backs up into the ureter and collecting system. The ureter and pelvis appear mildly dilated, and the calyces are mildly blunted.
- Grade IV: Urine backs up into the ureter and collecting system. The ureter and pelvis appear moderately dilated, and the calyces are moderately blunted.
- Grade V: Urine backs up into the ureter and collecting system. The pelvis severely dilates, the ureter appears tortuous, and the calyces are severely blunted.

Artificial Urinary Sphincter (AUS) (C1815, 53445, 53446, 53447, 53449)
The implantation of an artificial urinary sphincter (AUS) may be considered **medically necessary** in individuals following prostate surgery (post-proctectomy) for the treatment of urinary incontinence (UI) due to intrinsic sphincter deficiency (ISD) when the symptoms of urinary incontinence (UI) have been refractory to at least 6 months of conservative therapy: bladder training, prompted voiding, or pelvic muscle exercise training and pharmacological therapies.

Note: The implantation of an artificial urinary sphincter (AUS) is not considered first-line treatment of refractory urinary incontinence (UI) in members following prostate surgery. Examples of first-line conservative therapy may include one or more of the following: behavioral therapy, pharmacologic treatments, and intermittent self-catheterization.

The implantation of an artificial urinary sphincter (AUS) may be considered **not medically necessary** not meeting the above criteria and for all other indications.

Posterior Tibial Nerve Stimulation (PTNS) (64566, 0587T, 0588T, 0589T, 0590T)
Posterior tibial nerve stimulation (PTNS) (also known as percutaneous tibial nerve stimulation) for an initial 12-week course may be considered **medically necessary** for individuals with non-neurogenic urinary dysfunction* including overactive bladder (OAB) who have **ALL** the following:

- failed behavioral therapy following an appropriate duration of 8 to 12 weeks without meeting treatment goals; **and**
- failed pharmacologic therapy following 4 to 8 weeks of treatment without meeting treatment goals

Maintenance therapy using monthly posterior tibial nerve stimulation (PTNS) (also known as percutaneous tibial nerve stimulation) may be considered **medically necessary** for individuals following a 12-week initial course of posterior tibial nerve stimulation (PTNS) (also known as posterior tibial nerve stimulation) that resulted in improved urinary dysfunction meeting treatment goals.

Note: Annual evaluation by a physician may be performed to ensure efficacy is continuing for maintenance posterior tibial nerve stimulation (PTNS) (also known as percutaneous tibial nerve stimulation).

Notes:

- *Common causes of non-neurogenic voiding dysfunction are pelvic floor neuromuscular changes (e.g., from pregnancy, childbirth, surgery), inflammation, medication (e.g., diuretics, anticholinergics), obesity, and psychogenic factors. Overactive bladder is a non-neurogenic voiding dysfunction characterized by urinary frequency, urgency, urge incontinence, and nonobstructive retention.
- Neurogenic bladder dysfunction is caused by neurologic damage in patients with multiple sclerosis, spinal cord injury, detrusor hyperreflexia, or diabetes with peripheral nerve involvement. The symptoms include overflow incontinence, frequency, urgency, urge incontinence, and retention.

Posterior tibial nerve stimulation (PTNS) (also known as percutaneous tibial nerve stimulation) not meeting the above criteria and for all other indications is considered **not medically necessary.**

Note: *For Posterior tibial nerve stimulation (PTNS) (also known as percutaneous tibial nerve stimulation) for the treatment of fecal incontinence see medical policy 02.01.51 Fecal Incontinence Management which denies investigational for this indication.*

Investigational Therapies for the Treatment of Urinary Incontinence/Urinary Dysfunction

The following treatments and devices are considered **investigational** for the treatment of urinary incontinence/urinary dysfunction due to the lack of clinical evidence demonstrating an impact on improved net health outcomes:

- Laser therapy (Genityte procedure)
- Pelvic floor stimulation by any method electrical or magnetic (ExMI) (E0740)
  - ApexM™
  - Detrusan™
  - Elitone Device™
  - EmbaGYN®
  - Incare® PRS
  - MyoTrac Infiniti™
  - Pathway™ CTS2000
  - UROSTYM™
- Tactile biomechanical sensor imaging (transvaginal biomechanical imaging)
- The inFlow intraurethral valve-pump implantation (0596T, 0597T)
- Transperineal Implantation of Permanent Adjustable Balloon Continence Device (ProACT) (53451, 53452, 53453, 53454)
- Transvaginal and transurethral radiofrequency energy therapies for bladder neck suspension, including, but not limited to, the Lyrette Transurethral SUI System

(previously known as Renessa System), and the SURx Radiofrequency Bladder Neck Suspension System (53860)

- Vaginal weight training with specially designed weights (cones)

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- C1815 Prosthesis, urinary sphincter (implantable)
- E0740 Incontinence treatment system, pelvic floor stimulator, monitor, sensor, and/or trainer
- E1399 Durable Medical Equipment, miscellaneous (may be utilized for Attain Urinary Incontinence Device)
- L8603 Injectable bulking agent, collagen implant, urinary tract, 2.5 ml syringe, includes shipping and necessary supplies (Cross-Linked Collagen Bulking Agents)
- L8604 Injectable bulking agent, dextranomer/hyaluronic acid copolymer implant, urinary tract, 1 ml, includes shipping and necessary supplies (Deflux)
- L8606 Injectable bulking agent, synthetic implant, urinary tract, 1 ml syringe, includes shipping and necessary supplies (Durasphere, Coaptite, Macroplastique, Blukamid, Uryx)
- 51715 Endoscopic injection of implant material into the submucosal tissues of the urethra and/or bladder neck
- 52327 Cystourethroscopy (including ureteral catheterization); with subureteric injection of implant material
- 53445 Insertion of inflatable urethral/bladder neck sphincter, including placement of pump, reservoir, and cuff
- 53446 Removal of inflatable urethral/bladder neck sphincter, including pump, reservoir, and cuff
- 53447 Removal and replacement of inflatable urethral/bladder neck sphincter including pump, reservoir, and cuff at the same operative session
- 53449 Repair of inflatable urethral/bladder neck sphincter including pump, reservoir, and cuff
- 53451 Periurethral transperineal adjustable balloon continence device; bilateral insertion, including cystourethroscopy and imaging guidance (ProACT System)
- 53452 Periurethral transperineal adjustable balloon continence device; unilateral insertion, including cystourethroscopy and imaging guidance (ProACT System)
- 53453 Periurethral transperineal adjustable balloon continence device; removal, each balloon (ProACT System)

  53454 Periurethral transperineal adjustable balloon continence device; percutaneous adjustment of balloon(s) fluid volume (ProACT System)
- 53860 Transurethral, radiofrequency micro-remodeling of the female bladder neck and proximal urethra for stress urinary incontinence

- 53899 Unlisted procedure, urinary system (may be indicated for ExMi)
- 58999 Unlisted procedure, female genital system (nonobstetrical) (may be indicated for ExMi),
- 64566 Posterior tibial neurostimulation, percutaneous needle electrode, single treatment, includes programming
- 97014 Application of a modality to 1 or more areas; electrical stimulation (unattended)
- 97032 Application of a modality to 1 or more areas; electrical stimulation (manual), each 15 minutes
- 97039 Unlisted modality (specify type and time if constant attendance) (may be indicated for Vaginal weight training with specially designed weights [cones])
- 0587T Percutaneous implantation or replacement of integrated single device neurostimulation system including electrode array and receiver or pulse generator, including analysis, programming, and imaging guidance when performed, posterior tibial nerve
- 0588T Revision or removal of integrated single device neurostimulation system including electrode array and receiver or pulse generator, including analysis, programming, and imaging guidance when performed, posterior tibial nerve
- 0589T Electronic analysis with simple programming of implanted integrated neurostimulation system (e.g., electrode array and receiver), including contact group(s), amplitude, pulse width, frequency (Hz), on/off cycling, burst, dose lockout, patient-selectable parameters, responsive neurostimulation, detection algorithms, closed-loop parameters, and passive parameters, when performed by physician or other qualified health care professional, posterior tibial nerve, 1-3 parameters
- 0590T Electronic analysis with complex programming of implanted integrated neurostimulation system (e.g., electrode array and receiver), including contact group(s), amplitude, pulse width, frequency (Hz), on/off cycling, burst, dose lockout, patient-selectable parameters, responsive neurostimulation, detection algorithms, closed-loop parameters, and passive parameters, when performed by physician or other qualified health care professional, posterior tibial nerve, 4 or more parameters
- 0596T Temporary female intraurethral valve-pump (i.e., voiding prosthesis); initial insertion, including urethral measurement (inFlow intraurethral valve-pump implantation)
- 0597T Temporary female intraurethral valve-pump (i.e., voiding prosthesis); replacement (inFlow intraurethral valve-pump implantation)

SELECTED REFERENCES

- ECRI. Implantable Sacral Nerve Stimulator for Urinary Dysfunction. Plymouth Meeting (PA): ECRI Health Technology Information Service; 2006 August 17. 8p. (ECRI Hotline Response) Also available: http://www.ecri.org.

- ECRI. Injectable Urethral Bulking Agents for the Treatment of Urinary Stress Incontinence. Plymouth Meeting (PA): ECRI Health Technology Information Service; 2006 September 22. 11p. (ECRI Hotline Response) Also available: http://www.ecri.org.
- ECRI. Sling Systems for Female Urinary Stress Incontinence. Plymouth Meeting (PA): ECRI Health Technology Information Service; 2006 October 25. 13p. (ECRI Hotline Response) Also available: http://www.ecri.org.
- ECRI. Nonsurgical, Transurethral Radiofrequency Collagen Denaturation for Female Stress Urinary Incontinence. Plymouth Meeting (PA): ECRI Health Technology Information Service; 2007 August 10. 6p. (ECRI Hotline Response) Also available: http://www.ecri.org.
- Elser, DM, Mitchell, GK, Miklos, JR, Nickell, KG, Cline, K, Winkler, H, and Wells, WG. Nonsurgical transurethral collagen denaturation for stress urinary incontinence in women: 12-month results from a prospective long-term study. J Minim Invasive Gynecol. 2009;16(1):56-62.
- Davila, GW. Nonsurgical outpatient therapies for the management of female stress urinary incontinence: long-term effectiveness and durability. Adv Urol. 2011;2011:176498.
- Elser DM, Mitchell GK, Miklos JR, et al. Nonsurgical transurethral collagen denaturation for stress urinary incontinence in women: 18-month results from a prospective long-term study. Neurourol Urodyn. 2010 Nov;29(8):1424-8.
- ECRI. Nonsurgical, Transurethral Radiofrequency Collagen Denaturation for Female Stress Urinary Incontinence. Plymouth Meeting (PA):ECRI Health Technology Information Service;2010 Aug 24. (ECRI Hotline Service) Also available: http://www.ecri.org.
- Lucas MG, Bosch RJ, Burkhard FC, et al. EAU Guidelines on Surgical Treatment of Urinary Incontinence. Eur Urol. 2012 Sep 17. [Epub ahead of print]
- Shamliyan T, Wyman J, Kane RL. Nonsurgical Treatments for Urinary Incontinece in Adult Women: Diagnosis and Comparative Effectiveness. Pub. No. 11(12)-EHC074-EF. Rockville (MD): Agency for Healthcare Research and Quality (US). Comparative Effectiveness Review; April 2012.
- National Institute for Health and Clinical Excellence (NICE). Urinary incontinence in neurological disease. Clinical guideline 148; August 2012. Available at: http://www.guidance.nice.org.uk/cg148.
- Ghoniem GM & Miller CJ. A systematic review and meta-analysis of Macroplastique for treating female stress urinary incontinence. Int Urogynecol J. 2012 Jun 15. [Epub ahead of print]
- Pradhan A, Jain P, Latthe PM. Effectiveness of midurethral slings in recurrent stress urinary incontinence: a systematic review and meta-analysis. Int Urogynecol J. 2012 Jul;23(7):831-41.
- Monga AK, Tracey MR, Subbaroyan J. A systematic review of clinical studies of electrical stimulation for treatment of lower urinary tract dysfunction. Int Urogynecol J. 2012 Aug;23(8):993-1005.

- Greer JA, Smith AL, Arya LA. Pelvic floor muscle training for urgency urinary incontinence in women: a systematic review. Int Urogynecol J. 2012 Jun;23(6):687-97.
- Gormley EA, Lightner DJ, Burgio KL, et al. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline. 2012 May. 36 p.
- Agency for Healthcare Research and Quality (AHRQ). Nonsurgical Treatments for Urinary Incontinece in Adult Women: Diagnosis and Comparative Effectiveness. Pub. No. 11(12)-EHC074-EF. Prepared by Minnesota Evidence-based Practice Center, Minneapolis MN; April 2012.
- ECRI. Posterior Tibial Nerve Stimulation for Treating Urge Incontinence. Plymouth Meeting (PA): ECRI Health Technology Information Service; 3/20/12.[Hotling Response]. Available at: http://www.ecri.org.
- Deflux-product insert, Oceana Therapeutics. Accessed 9/16/13 www.deflux.com.
- Committee on Gynecologic Practice, guideline recommendation Nuber 603. June 2014.
- U.S. Food and Drug Administration (FDA). Center for Devices and Radiological Health (CDRH). 510(k) Summary of Safety and Effectiveness. AMS Sphincter 800™ Urinary Prosthesis. No. P000053. Rockville, MD: FDA. June 14, 2001. Available at: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfTopic/pma/pma.cfm?num=P000053.
- Islah M, Cho SY, Son H. The current role of the artificial urinary sphincter in male and female urinary incontinence. World J Mens Health. 2013; 31(1):21-30. Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3640149/.
- O'Connor RC, Nanigian DK, Patel BN, et al. Artificial urinary sphincter placement in elderly men. Urology. 2007 Jan; 69(1): 126-8.
- Sand, PK., Owens, GM., Black, EJ., Anderson, LH., Martinson, MS. Cost=effectiveness of radiofrequency microremodeling for stress urinary incontinence. Int Urogynecol. 2014; 25(4): 517-23.
- Lukban, JC. Transureethral radiofrequency collagen denaturation for treatment of female stress urinary incontinence: a review of the literature and clinical recommendations. Obstet Gynecol Int. 2012.
- Shamliyan T, Wyman J, Kane RL. Nonsurgical Treatments for Urinary Incontinence in Adult Women: Diagnosis and Comparative Effectiveness. Comparative Effectiveness Review No. 36. (Prepared by the University of Minnesota Evidence-based Practice Center under Contract No. HHSA 290-2007-10064-I.) AHRQ Publication No. 11(12)-EHC074-EF. Rockville, MD. Agency for Healthcare Research and Quality. April 2012
- Moroni RM, Magnani PS, Haddad JM, et al. Conservative treatment of stress urinary incontinence: a systematic review with meta-analysis of randomized controlled trials. Rev Bras Ginecol Obstet. Feb 2016;38(2):97-111. PMID 26883864
- Hsu LF, Liao YM, Lai FC, et al. Beneficial effects of biofeedback-assisted pelvic floor muscle training in patients with urinary incontinence after radical

prostatectomy: A systematic review and metaanalysis. Int J Nurs Stud. Aug 2016;60:99-111. PMID 27297372
- Starr,J., Drobnis, E., Lenger,S., Parrot, J., Barrier, B., Foster, R.,(2013). Outcomes of a comprehensive nonsurgical approach to pelvic floor rehabilitation for urinary symptoms, defecatory dysfunction, and pelvic pain. *Female Pelvic Medicine and Reconstructive Surgery.* 95, 260-264.
- U.S. Food and Drug Administration (FDA). Summary of Safety and Effectiveness. ProACT™ Adjustable Continence Therapy for Men. No. P130018. Rockville, MD: FDA. November 24, 2015. Available at: https://www.accessdata.fda.gov/cdrh_docs/pdf13/P130018B.pdf .
- U.S. Food and Drug Administration (FDA). inFlow™ Intraurethral Valve-Pump approval. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf13/den130044.pdf.
- ECRI Institute. ProACT Adjustable Continence Therapy for Treating Male Stress Urinary Incontinence. May 2018, Available at: http://www.ecri.org.
- Pergialiotis V, Prodromidou A, Perrea DN, Doumouchtsis SK. A systematic review on vaginal laser therapy for treating stress urinary incontinence: Do we have enough evidence? Int Urogynecol J. 2017;28(10):1445-1451.
- Rodrigues MP, Paiva LL, Ramos JGL, Ferla L. Vibratory perineal stimulation for the treatment of female stress urinary incontinence: A systematic review. Int Urogynecol J. 2017 Aug 15 [Epub ahead of print].
- Deegan EG, Stothers L, Kavanagh A, Macnab AJ. Quantification of pelvic floor muscle strength in female urinary incontinence: A systematic review and comparison of contemporary methodologies. Neurourol Urodyn. 2018;37(1):33-45.
- Song P, Wen Y, Huang C, et al. The efficacy and safety comparison of surgical treatments for stress urinary incontinence: A network meta-analysis. Neurourol Urodyn. 2018 Jan 13 Epub ahead of print].
- Chapple CR, Cruz F, Deffieux X, et al.(2017) Consensus Statement of the European Urology Association and the European Urogynaecological Association on the Use of Implanted Materials for Treating Pelvic Organ Prolapse and Stress Urinary Incontinence. Eur Urol. Apr 13 2017. PMID 28413126
- Kobashi KC, Albo ME, Dmochowski RR, et al.(2017) Surgical Treatment of Female Stress Urinary Incontinence: AUA/SUFU Guideline. J Urol. Jun 15 2017. PMID 28625508
- Nambiar AK, Bosch R, Cruz F, et al.(2018) EAU guidelines on assessment and nonsurgical management of urinary incontinence. Eur Urol. Apr 2018;73(4):596-609. PMID 29398262
- Zhang J, Gao L, Liu M, Liu C. Effect of bariatric surgery on urinary incontinence in obese women: A meta-analysis and systematic review. Female Pelvic Med Reconstr Surg. 2018 Aug 31 [Epub ahead of print].
- Tutolo, Manuela et al. What Is New in Neuromodulation for Overactive Bladder? European Urology Focus, Volume 4, Issue 1, 49 - 53

- Nelson HD, Cantor A, Pappas M, Miller L. Screening for urinary incontinence in women: A systematic review for the women's preventive services initiative. Ann Intern Med. 2018;169(5):311-319.
- Chung E. Artificial urinary sphincter surgery in the special populations: neurological, revision, concurrent penile prosthesis and female stress urinary incontinence groups. Asian J Androl 2020;22:45-50
- Peyronnet B, Capon G, Belas O, Manunta A, Allenet C, et al. Robot-assisted AMS-800 artificial urinary sphincter bladder neck implantation in female patients with stress urinary incontinence. Eur Urol 2019; 75: 169–75
- Lin HY, Tsai HW, Tsui KH, et al. The short-term outcome of laser in the anagement of female pelvic floor disorders: Focus on stress urine incontinence and sexual dysfunction. Taiwan J Obstet Gynecol. 2018;57(6):825-829.
- Gonzalez Isaza P, Jaguszewska K, Cardona JL, Lukaszuk M. Longterm effect of thermoablative fractional CO2 laser treatment as a novel approach to urinary incontinence management in women with genitourinary syndrome of menopause. Int Urogynecol J. 2018;29(2):211-215.
- Peng L, Zeng X, Shen H, Luo DY. Magnetic stimulation for female patients with stress urinary incontinence, a meta-analysis of studies with short-term follow-up. Medicine (Baltimore). 2019;98(19):e15572.
- American Urological Association (2019) Diagnosis and Treatment of Non-Neurogenic Overactive Bladder (OAB) in Adults: an AUA/SUFU Guideline. https://www.auanet.org/guidelines/overactive-bladder-(oab)-guideline
- UpToDate**.** Treatment of Urinary Incontinence in Females. Emily S. Luckaz M.D., MAS, topic last updated October 19, 2020. Also available at https://www.uptodate.com
- UpToDate. Urinary incontinence in men. L Quentin Clemens M.D., FACS, MSCI topic last updated December 2, 2019. Also available at https://www.uptodate.com
- UpToDate. Urgency urinary incontinence/overactive bladder (OAB) in females: Treatment. Topic last updated May 18, 2021. Also available at https://www.uptodate.com
- Ramirez-Garcia I, Blanco-Ratto L, Kauffmann S, et. al. Efficacy of transcutaneous stimulation of the posterior tibial nerve compared to percutaneous stimulation in idiopathic overactive bladder syndrome: randomized control trial. Neurourol Urodyn 2019 Jan;38(1):261-268. PMID 30311692
- Tutolo M, Ammirati E, Van der Aa F. What is new in neuromodulation for overactive bladder? Eur Urol Focus 2018 Jan;4(1):49-53. PMID 29773501
- Zonic-Imamovic M, Immaovic, Cickusic A, et. al. Effects of treating an overactive urinary bladder in patients with Multiple Sclerosis. Acta Med Acad 2019 Dec;48(3):271-277. PMID 32124625
- Welk B. McKibbon M. A randomized, controlled trial of transcutaneous tibial nerve stimulation to treat overactive bladder and neurogenic bladder patients. Can Urol Assoc J. 2020 Jul;14(7):E297-E303. PMID 32017693

- Kavanagh A, Baverstock R, Campeau L et. al. Canadian Urological Association guideline: Diagnosis, management, and surveillance of neurogenic lower urinary tract dysfunction. Can Urol Assoc J. 2019 Jun;13(6): E157-E176. PMID 30763235
- Marcelissen T, Cornu JN, Antunes-Lopes T, et. al. Management of idiopathic overactive bladder syndrome: what is the optimal strategy after failure of conservative treatment? Eur Urol Focus 2018 Sep;4(5):760-767. PMID 29807823
- Boswell T, Elliott D, Rangel L, et. al. Long-term device survival and quality of life outcomes following artificial urinary sphincter placement. Transl Androl Urol 2020 Feb;9(1):56-61. PMID 32055467
- Capobianco G, Saderi L, Dessole F, et. al. Efficacy and effectiveness of bulking agents in the treatment of stress and mixed urinary incontinence: a systematic review and meta-analysis. Maturitas 2020 Mar;133:13-31. PMID 32005420
- Bomba P, Florez F, Garcia F, et. al. Effectiveness of surgical management with an adjustable sling versus an artificial urinary sphincter in patients with severe urinary post-prostatectomy incontinence: a systematic review and network meta-analysis. Ther Adv Urol 2019 Jan-Dec; 11 PMID 31632464
- Sacomani C, Zequi S, da Costa W, et. al. Long-term results of the implantation of the AMS 800 artificial sphincter for post-prostatectomy incontinence: a single-center experience. Int Braz J Urol 2018 Jan-Feb 44(1):114-120. PMID 29211407
- Tutolo M, Cornu JN, Bauer R, et. al. Efficacy and safety of artificial urinary sphincter (AUS): Results of a large multi-institutional cohort of patients with mid-term follow-up. Neurourol Urondyn 2019 Feb;38(2):710-718. PMID 30575997
- Kirchin V, Page T, Keegan P, et. al. Uretheral injection therapy for urinary incontinence in women. Cochran Database Syst Rev 2017 Jul;2017(7). PMID 28738443
- Kobashi KC, Albo ME, Dmochowski RR, et. al. Surgical treatment of female stress urinary incontinence (SUI): AUA/SUFU Guideline (2017). J Urol 2017;198:875
- Deflux. https://deflux.com
- Bulkamid FDA approval
- Uryx FDA approval
- Elitone Device
- Stewart F, Berghmans B, Bo K, et al. Electrical stimulation with non-implanted devices for stress urinary incontinence in women. Cochrane Database Syst Rev. Dec 22 2017; 12: CD012390. PMID 29271482
- Sciarra A, Viscuso P, Arditi A, et al. A biofeedback-guided programme or pelvic floor muscle electric stimulation can improve early recovery of urinary continence after radical prostatectomy: A meta-analysis and systematic review. Int J Clin Pract. Apr 02 2021: e14208. PMID 33811418
- Sandhu JS, Breyer B, Comiter C, et al. Incontinence after Prostate Treatment: AUA/SUFU Guideline. J Urol. Aug 2019; 202(2): 369-378. PMID 31059663
- Mateus-Vasconcelos ECL, Ribeiro AM, Antonio FI, et al. Physiotherapy methods to facilitate pelvic floor muscle contraction: A systematic review. Physiother Theory Pract. Jun 2018; 34(6): 420-432. PMID 29278967

- Oh JJ, Kim JK, Lee H, et al. Effect of personalized extracorporeal biofeedback device for pelvic floor muscle training on urinary incontinence after robot-assisted radical prostatectomy: A randomized controlled trial. Neurourol Urodyn. Feb 2020; 39(2): 674-681. PMID 31793032
- 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
- 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
- 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
- Wang M, Jian Z, Ma Y, et al. Percutaneous tibial nerve stimulation for overactive bladder syndrome: a systematic review and meta-analysis. Int Urogynecol J. Dec 2020; 31(12): 2457-2471. PMID 32681345
- Xiong SC, Peng L, Hu X, et al. Effectiveness and safety of tibial nerve stimulation versus anticholinergic drugs for the treatment of overactive bladder syndrome: a meta-analysis. Ann Palliat Med. Jun 09 2021. PMID 34118839
- Coolen RL, Groen J, Scheepe JR, et al. Transcutaneous Electrical Nerve Stimulation and Percutaneous Tibial Nerve Stimulation to Treat Idiopathic Nonobstructive Urinary Retention: A Systematic Review. Eur Urol Focus. Oct 22 2020. PMID 33268327
- Ho FCS, He C, Yao HH, et al. Efficacy of sacral neuromodulation and percutaneous tibial nerve stimulation in the treatment of chronic nonobstructive urinary retention: A systematic review. Neurourol Urodyn. Jun 2021; 40(5): 1078-1088. PMID 33973670
- Tutolo M, Ammirati E, Heesakkers J, et al. Efficacy and Safety of Sacral and Percutaneous Tibial Neuromodulation in Non-neurogenic Lower Urinary Tract Dysfunction and Chronic Pelvic Pain: A Systematic Review of the Literature. Eur Urol. Mar 2018; 73(3): 406-418. PMID 29336927
- Tutolo M, Ammirati E, Van der Aa F. What Is New in Neuromodulation for Overactive Bladder?. Eur Urol Focus. Jan 2018; 4(1): 49-53. PMID 29773501
- Zonic-Imamovic M, Imamovic S, Cickusic A, et al. Effects of Treating an Overactive Urinary Bladder in Patients with Multiple Sclerosis. Acta Med Acad. Dec 2019; 48(3): 271-277. PMID 32124625
- Welk B, McKibbon M. A randomized, controlled trial of transcutaneous tibial nerve stimulation to treat overactive bladder and neurogenic bladder patients. Can Urol Assoc J. Jul 2020; 14(7): E297-E303. PMID 32017693

POLICY HISTORY		
Date	**Reason**	**Action**
July 2022	Interim Review	Policy Revised
June 2022	Annual Review	Policy Revised
April 2022	Interim Review	Policy Revised
June 2021	Annual Review	Policy Revised
June 2020	Annual Review	Policy Revised
June 2019	Annual Review	Policy Revised
June 2018	Annual Review	Policy Revised
June 2017	Annual Review	Policy Revised
July 2016	Annual Review	Policy Revised
July 2015	Annual Review	Policy Revised
August 2014	Annual Review	Policy Renewed
May 2014	Interim Review	Policy Revised
September 2013	Annual Review	Policy Revised
October 2012	Annual Review	Policy Renewed
October 2011	Annual Review	Policy Renewed
September 2010	Annual Review	Policy Renewed

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
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