Medical Coverage Policy

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Sacral Nerve and Tibial Nerve Stimulation for Urinary Voiding Dysfunction, Fecal Incontinence and Constipation

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Overview

This Coverage Policy addresses sacral nerve stimulation (SNS), percutaneous tibial nerve stimulation (PTNS) and implantable tibial nerve stimulation as a treatment for the involuntary leakage of urine or stool and constipation.

Coverage Policy

Sacral Nerve Stimulation (SNS)

Urinary Voiding Dysfunction

A screening trial of sacral nerve stimulation (SNS) with an external stimulator for either percutaneous nerve evaluation (PNE) or an implanted lead is considered medically necessary for the treatment of any of the following urinary voiding dysfunctions when there is failure, intolerance or contraindication to conservative medical management:

- urinary urge incontinence
- nonobstructive urinary retention
- overactive bladder (OAB) symptoms, including urinary frequency and/or urgency, with or without incontinence

Permanent SNS implantation for the treatment of urinary voiding dysfunction is considered medically necessary when there has been a beneficial clinical response to a screening trial of SNS as evidenced by at least a 50% improvement in reported symptoms.

Fecal Incontinence

A screening trial of sacral nerve stimulation (SNS) with an external stimulator for either percutaneous nerve evaluation (PNE) or an implanted lead is considered medically necessary for the treatment of fecal incontinence when ALL of the following criteria are met:

- failure, intolerance, or contraindication to conservative medical management
- absence of a significant anorectal malformation or chronic inflammatory bowel disease involving the anus
- fecal incontinence is not secondary to another neurological condition such as peripheral neuropathy or complete spinal cord injury

Permanent SNS implantation for fecal incontinence is considered medically necessary when there has been a beneficial clinical response to a screening trial of SNS as evidenced by at least a 50% improvement in reported symptoms.

The replacement/revision of a sacral nerve stimulator generator/battery and/or lead/electrode and/or patient programmer is considered medically necessary for an individual who meets ALL of the above criteria and the existing generator/lead/programmer is no longer under warranty and cannot be repaired.

SNS for the treatment of any other indication, including constipation is considered experimental, investigational or unproven.

Percutaneous Tibial Nerve Stimulation (PTNS)

Overactive Bladder

A standard treatment regimen of 30-minute weekly sessions for 12 weeks of percutaneous tibial nerve stimulation (PTNS) is considered medically necessary for the treatment of overactive bladder (OAB) symptoms when there is failure, intolerance, or contraindication to conservative medical management (e.g., bladder training, pharmacotherapy).

Implantable Tibial Nerve Stimulation

Implantable tibial nerve stimulation for the treatment of urinary voiding dysfunction (e.g., overactive bladder, urinary urge incontinence), fecal incontinence and constipation is considered experimental, investigational or unproven.

General Background

Sacral Nerve Stimulation (SNS)

Sacral nerve stimulation (SNS), also known as sacral nerve neuromodulation, involves the implantation of a permanent device that modulates the neural pathways. The exact mechanism of action is unclear (Abello and Das, 2018). Sacral nerve stimulation (SNS) applies a low amplitude electrical current to a sacral nerve through an electrode that is placed through a corresponding sacral foramen. The stimulation of the sacral nerves leads to recruitment of the pelvic floor musculature and pelvic organs, leading to improvement in pelvic floor function. The third sacral foramen is the level at which an optimal response is most commonly elicited. The third sacral nerve root contains afferent sensory and efferent autonomic motor nerves and voluntary somatic fibers, which may, alone or in harmony, create the beneficial effect elicited by SNS (Mellgren, 2010).

Syan et al. (2020) conducted study that analyzed if racial and socioeconomic factors influenced the utilization of advanced therapies in commercially insured OAB Patients. Through a query of Optum, a national claims database, they found that Asians and Hispanics were least likely to utilize SNS therapy and most likely to use PTNS compared to Blacks and Whites. Female gender, younger age (< 65), higher annual income ≥ $40K and prior use of oral medications were significantly associated with receiving advanced therapies. In addition, non-white race, lower education level (less than a bachelor's degree) and Northeast region were associated with a lower likelihood of receiving advanced therapies ($p<0.05$ for all).

Prior to the implantation of a permanent SNS system, patients are screened for potential therapeutic benefit by undergoing a screening trial period. There are two methods that can be used for screening prior to permanent implantation, a percutaneous nerve evaluation (PNE) or a

two staged implantation approach. During a PNE, a non-anchored test lead is placed percutaneously at the sacral nerve site using a lead introducer, and then a percutaneous lead extension is connected to an external test stimulator. The external test stimulator device provides continuous stimulation. Following an adequate test period for efficacy or lack, thereof (efficacy defined as a ≥50% subjective and/or objective response), the electrode is removed. If the screening trial is successful, a permanent lead and implantable pulse generator (IPG) may be placed in the operating room (Hassouna and Alabbad, 2018; Abello and Das, 2018).

The two staged implantation method is indicated for patients who fail PNE, for patients with an inconclusive PNE, for patients who had a successful PNE to refine patient selection further or instead of PNE. During the first stage, a permanent quadripolar tined lead is implanted, connected subcutaneously to a temporary extension lead and then connected to an external pulse generator. If the trial is successful, a second-stage procedure is done for placement of the permanent IPG. The trial period can vary between three days and up to two weeks. Shorter trials are typically done with PNE (3–5 days), while the longer trial periods up to two weeks can be done with the tined lead as it has a lower risk of lead migration. Complications to SNS include device-related pain, need for revision, infection, and neurologic complications (Hassouna and Alabbad, 2018; Abello and Das, 2018).

SNS has been proposed for the treatment of urinary voiding dysfunction, including intractable urinary urge incontinence, nonobstructive urinary retention, urinary urgency/frequency, fecal incontinence, and several other indications.

Urinary Voiding Dysfunction
Urinary voiding dysfunction is usually defined as the inability to control urination. Urinary voiding disorders are generally divided into five types, depending on the pathophysiology involved: urge incontinence-a subtype is urgency-frequency syndrome, overflow incontinence, stress incontinence, mixed incontinence, functional incontinence.

Treatment options for urinary voiding disorders may include behavioral strategies, pharmacological interventions, temporary electrical stimulation, or reconstructive surgery. Less invasive modalities are generally used initially before irreversible, reconstructive surgery is considered.

Sacral nerve stimulation (SNS) may be indicated in patients who demonstrate at least 50% urinary incontinence symptom relief during test stimulation and who have failed or not tolerated more conservative treatments (e.g., behavioral strategies, pharmacological interventions). The criteria for a positive response vary slightly; however, at least a 50% improvement in one or more primary symptoms is considered the standard for a clinically significant response (Schmidt, 1999). It is not proposed for the treatment of stress incontinence, the most common type of urinary dysfunction (Hassouna, 2000).

The precise mode of action of neuromodulation on the lower urinary tract is unclear. When a nerve is stimulated, signals travel both toward the periphery and toward the central nervous system (Herbison, 2009). According to the manufacturer of the InterStim® System for Urinary Control (Medtronic, Inc., Minneapolis, MN), SNS is not intended for patients with mechanical obstruction such as benign prostatic hypertrophy, cancer, or urethral stricture. Medtronic also states that the safety and effectiveness of SNS has not been established for bilateral stimulation, patients with neurological disease origins (e.g., multiple sclerosis), pregnancy and delivery or for children under the age of 16 (Medtronic, Inc., 2019).

Sacral nerve stimulation is considered an appropriate treatment option for individuals with refractory voiding dysfunction, with failure of, or contradiction or intolerance to conservative medical management after a 50% improvement is noted in response to a screening trial.

U.S. Food and Drug Administration (FDA): In 1997, the InterStim® Therapy System for Urinary Control (Medtronic, Inc., Minneapolis, MN) received premarket approval from the FDA "for the treatment of urinary urge incontinence in patients who have failed or could not tolerate more conservative treatments". In 1999, a supplement expanded the indication to include "urinary retention, and significant symptoms of urgency/frequency". In August 2001, the FDA approved the Model 3550-03 Twist-Lock Screening Cable and Model 3550-05 Percutaneous Extension and Tunneling Tool Kit for temporary SNS as part of a staged implant screening technique for patients who had inconclusive results following standard percutaneous testing. A supplement in 2002, granted approval for the revised indication: "InterStim Therapy for Urinary Control is indicated for the treatment of urinary retention and the symptoms of overactive bladder, including urinary urge incontinence and significant symptoms of urgency-frequency alone or in combination, in patients who have failed or could not tolerate more conservative treatments". A supplement in 2020 (P970004/S302), granted approval for the InterStim Micro System with full-body MR conditional labeling, which is an updated version of the InterStim II System. The modifications include new SureScan MRI leads, an updated Verify Evaluation System that can accommodate newly developed leads, and related labeling updates (FDA, 2020). A supplement in 2022 (P970004/S340), granted approval for the InterStim X INS that features more than 10 years of battery life without the need to recharge, with low energy settings, the device can last up to 15 years (FDA, 2022; Medtronic, 2022).

In 2019, the Axonics Sacral Neuromodulation System (Axonics Modulation Technologies, Inc., Irvine, California) received premarket approval from the FDA "for the treatment of urinary retention and the symptoms of overactive bladder, including urinary urge incontinence and significant symptoms of urgency-frequency alone or in combination, in patients who have failed or could not tolerate more conservative treatments" (FDA, 2019a).

Literature Review - Sacral Nerve Stimulation (SNS) for Urinary Voiding Dysfunction: Several randomized clinical trials (RCTs), prospective case series, retrospective analyses and systematic reviews have demonstrated > 50% improvement in incontinence symptoms, decrease in the number of daily catheterizations required, an increase in the volume of urine obtained per void, and a decrease in post-void residual urine volume with the use of sacral nerve stimulation (SNS) (Szymański, et al., 2019; Tutolo, et al., 2018; Noblett, et al., 2014; Herbison, 2009; White, 2008; van Kerrebroeck, 2007, Sutherland, 2007). Adverse events reported include changes in stimulation sensation, loss of efficacy, pain at the implantation site, and the need for intravenous antibiotics.

Siegel, et al. (2015) published their results of a post-approval RCT (n=147) comparing SNS (n=70) to standard medical therapy (n=77) for OAB. Inclusion criteria were failed or not a candidate for conservative treatment, including pharmacotherapy. Exclusion criteria included severe or uncontrolled diabetes, neurological diseases such as multiple sclerosis, clinically significant peripheral neuropathy or complete spinal cord injury (e.g., paraplegia), symptomatic urinary tract infection, and primary stress incontinence. All subjects were required to discontinue OAB medications for four days prior to their initial voiding diary. The primary outcome measure of OAB therapeutic success defined as 50% improvement in average leaks/day or voids/day from baseline or a return to normal voiding frequency (< 8 voids/day). Secondary outcomes included quality of life measures. A total of 59 patients from the SNS group and 71 patients from the standard medical therapy group (anticholinergic or antimuscarinic medication) completed six-month follow-up. For the primary outcome, 61% of SNS subjects demonstrated therapeutic success at six months versus 42% of the standard medical therapy subjects ($p<0.02$). The SNS

group also showed greater improvement in all domains of the quality-of-life scales compared to the standard medical therapy group ($p<0.001$). Adverse events related to the SNS device occurred in 30.5% (18/59) of subjects with a lead implant. OAB medication-related events occurred in 27.3% (21/77) of standard medical therapy subjects. Acknowledged study limitations include the homogeneous nature of the population and the lack of blinding. Study results suggested that SNS results in a greater reduction of OAB symptoms and improvement in quality-of-life indicators than standard medical therapy.

A systematic review by Herbison et al. (2009), evaluated twelve reports of eight randomized studies of 500 adults with urge urinary incontinence, overactive bladder syndrome (i.e., urgency or frequency), and urinary retention. About 50% of patients in the stimulation group achieved complete continence or an improvement greater than 90% of the main incontinence symptoms. Eighty-seven percent of patients achieved a 50% improvement. In all reports, participants had failed conventional treatments before randomization. It is unclear whether the studies all used the same implant. The authors noted that several long-term studies had poor rates of follow-up. Thirty percent or more potentially eligible patients were not implanted and 30% or more of those implanted did not gain benefit. Overall continuous stimulation offered benefits for carefully selected individuals with overactive bladder syndrome and for those with urinary retention but no structural obstruction.

Van Kerrebroeck et al. (2007) reported long-term results of a five-year prospective multi-center study that evaluated the safety and efficacy of SNS in patients with refractory urge incontinence, urgency frequency, and retention. One hundred sixty-three patients enrolled in the study and after undergoing test stimulation 152 underwent SNS implantation. Implanted devices varied between patients. Three-day voiding diaries were collected annually for five years-diary variables differed according to the type of urinary disorder. Simple uroflow and quality of life questionnaires, such as the Short Form-36 and the Beck Depression Inventory were used. Detailed data were also collected on any concomitant treatment for the urological condition and on any therapy or patient related complications. Clinical success was defined as ≥ 50% improvement in baseline. For patients with urge incontinence mean leaking episodes per day decreased from 9.6 to 3.9 at five years. For patients with urgency frequency, mean voids per day decreased from 19.3 to 14.8 and mean volume voided per void increased from 92.3 ml to 165.2 ml. For patients with retention the mean volume per catheterization decreased from 379.9 ml to 109.2 ml, and the mean number of catheterizations decreased from 5.3 to 1.9. All changes were statistically significant ($p<0.001$). No life threatening or irreversible adverse events occurred; however, in 102 patients 279 device or therapy related adverse events were observed. At five years after implantation, 68% of patients with urge incontinence, 56% with urgency frequency and 71% with retention had successful outcomes.

There is sufficient high quality controlled clinical trial data to demonstrate the safety and effectiveness of sacral nerve stimulation for the treatment of individuals with refractory voiding dysfunction, with failure of, or contradiction or intolerance to conservative medical management after a 50% improvement is noted in response to a percutaneous screening trial.

Fecal Incontinence

Fecal incontinence is the inability to control bowel movements leading to feces leaking from the rectum. The reported prevalence in the general population is 2% to 3%. Severe fecal incontinence can be socially isolating as an individual with the condition may alter his/her lifestyle to accommodate the likelihood of bowel leakage. Fecal incontinence may be caused by several factors including muscle damage, such as that experienced after childbirth, or after rectal surgery, or from damage to the nerves that control the anal muscle or regulate rectal sensation (Wald, 2016). Additionally, it may be caused by a reduction in the elasticity of the rectum, which shortens the time between the sensation of the stool and the urgent need to have a bowel movement.

Surgery or radiation injury can scar and stiffen the rectum. Inflammatory bowel disease can also make the rectum less elastic. Treatment depends on the cause of the incontinence and may include dietary changes, drug therapy, bowel training, or surgery. Surgical treatment options for fecal incontinence include an overlapping sphincter repair, total pelvic floor reconstruction or, less commonly, artificial bowel sphincters (Fargo & Latimer, 2012). Fecal incontinence remains a therapeutic problem in many patients when conservative measures, such as dietary advice, pelvic floor exercises and medical therapy with bulking agents, fails and sphincter repair is unsuccessful or inappropriate (Chan, 2008; Leroi, et al., 2005, Jarrett, et al., 2004). Sacral nerve stimulation (SNS) has been proposed for the treatment of fecal incontinence.

The exact mechanism of action of SNS for fecal incontinence remains unclear. According to Gladman (2008), "Although it was initially thought that SNS would directly augment anal sphincter function and improve fecal incontinence, the observation that improved continence occurs without change in anal sphincter function has led to the suggestion that SNS has predominantly suprasphincteric effects. The mechanism of action of SNS is not conclusively proved and may involve direct effects peripherally on colorectal sensory or motor function, or central effects at the level of spinal cord or brain." Further neurophysiological research is necessary to understand the mechanisms of sacral neuromodulation" (Melenhorst, et al., 2007).

Indications and patient selection for the use of sacral nerve stimulation (SNS) for the treatment of fecal incontinence continue to evolve. Initial study eligibility included patients with a functionally deficient but morphologically intact anal sphincter. More recently, inclusion criteria has been extended to include those with external and internal sphincter defects, secondary to cauda equina syndrome, scleroderma, rectal prolapse repair, low anterior resection of the rectum, and partial spinal injuries (Gladman, 2008; Jarrett, et al., 2004).

U.S. Food and Drug Administration (FDA): In March 2011, Medtronic, Inc. (Minneapolis, MN) received premarket approval from the FDA for the Medtronic InterStim® Sacral Nerve Stimulation Therapy System. This device is indicated for the treatment of chronic fecal incontinence in patients who have failed or are unable to tolerate more conservative treatments (FDA, 2011). A supplement in 2020 (P080025/S197), granted approval for the InterStim Micro System with full-body MR conditional labeling, which is an updated version of the InterStim II System. The modifications include new SureScan MRI leads, an updated Verify Evaluation System that can accommodate newly developed leads, and related labeling updates (FDA, 2020). A supplement in 2022 (P080025/235), granted approval for the InterStim X INS that features more than 10 years of battery life without the need to recharge, with low energy settings, the device can last up to 15 years (FDA, 2022; Medtronic 2022).

In 2019, the Axonics Sacral Neuromodulation System (Axonics Modulation Technologies, Inc., Irvine, California) received premarket approval from the FDA "for the treatment of chronic fecal incontinence in patients who have failed or are not candidates for more conservative treatments" (FDA, 2019b).

Literature Review - Sacral Nerve Stimulation (SNS) for Fecal Incontinence: Randomized controlled data is limited regarding the effects of SNS; however, there is sufficient evidence to support the use of SNS for the treatment of fecal incontinence following a successful screening trial. A number of prospective case series and retrospective reviews have noted improvements in the frequency of incontinence episodes and quality of life measures as self-reported in bowel diaries and quality of life scales (Rydningen, et al., 2017; Hull, et al., 2013; Damon, et al., 2013; Devroede, 2012; Boyle, et al., 2011; Mellgren, 2011; Uludag, et al., 2011; Michelson, et al., 2010; Wexner, et al., 2010; Matzel, et al., 2009; Meurette, et al., 2009; Chan, 2008).

In a prospective uncontrolled trial investigating the effectiveness of SNS for fecal incontinence, Wexner et al. (2010) evaluated 285 patients. One hundred thirty-three patients underwent peripheral nerve stimulation and 120 of those individuals received permanent SNS. Mean follow-up was 28 months. Study participants were requested to complete a five-question bowel diary at baseline, during test stimulation, and at three, six, and 12 months and annually after study closure. Quality of life and well-being were also assessed by additional questionnaires. At 12 months, 83% achieved therapeutic success defined as achieving ≥ 50% reduction in the number of incontinent episodes per week compared to the baseline; 85% achieved therapeutic success at 24 months. Forty percent of those receiving SNS achieved 100% improvement in incontinent episodes per week and incontinent days per week at 12 months. Incontinence episodes decreased from a mean of 9.4 per week at baseline to 1.9 at 12 months, and 2.9 at two years. Adverse event (AE) rates were high with 696 AEs reported. Three hundred seven AEs in 96 patients were related to the device or therapy. Twenty-six AEs were considered serious and included implant site pain, hematomas, lead fractures, lead migrations or dislodgments, extremity pain, skin irritation, paresthesia's, implant site infection, change in sensation of stimulation, urinary incontinence, and diarrhea. 10.8% of patients experienced implant site infection and 5.8% required surgical removal of the implant. Study limitations included an uncontrolled, nonrandomized design and short-term follow-up.

Mellgren et al. (2011) reported results of a three-year follow-up assessment of the trial by Wexner et al. Of 120 patients receiving chronic SNS, eighty-three patients completed part or all of the assessment, with 86% of patients reporting ≥ 50% reduction in the number of incontinent episodes per week compared with baseline. Perfect continence was reported by 40% of study participants. Improvements in the Fecal Incontinence Quality of Life scale were reported at 12, 24, and 36 months of follow-up. Device- or therapy-related adverse events included implant site pain (28%), paresthesia (15%), change in the sensation of stimulation (12%), and infection (10%). Limitations included an uncontrolled, nonrandomized study design.

Tan et al. (2011) performed a meta-analysis of thirty-four studies, including 944 patients undergoing peripheral nerve evaluation; 665 underwent permanent sacral nerve stimulation (SNS). Study design included twenty-eight prospective non-randomized trials; two retrospective trials, one prospective cross-sectional study, two double-blind cross-over trials, and a randomized controlled trial. Follow-up ranged from two weeks to 35 weeks. All studies reported on at least one outcome of interest. Studies were analyzed for functional outcomes (i.e., weekly incontinence episodes, Wexner (Cleveland) incontinence scores, and ability to defer defecation.), Quality of Life outcomes (i.e., SF-36 questionnaire), fecal incontinence quality of life (FIQL) questionnaire (the American Society of Colon and Rectal Surgery [ASCRS] quality of life questionnaire), anal manometry (i.e., resting and squeeze pressures), and rectal sensitivity (i.e., threshold, urge and maximum tolerable volumes). Regarding functional outcomes, twenty-eight studies reported on incontinence episodes per week; all studies reported a decrease following SNS, compared with conservative therapy ($p<0.001$). Sixteen studies reported at the time patients were able to defer defecation; seven of these were excluded from analysis as data were reported in groups. In the nine studies included in the analysis there was a significant increase in the ability to defer defecation following sacral nerve stimulation ([SNS], $p<0.001$). Regarding Quality of Life outcomes, there was an increase in the weighted mean difference of all SF-36 outcomes in favor of sacral nerve stimulation (SNS), with all but one (bodily pain, $p=0.13$) reaching significance. Overall, there was a significant increase in the SNS group in all subcategories of the FIQL questionnaire. In the studies included in the analysis for resting and squeeze pressure, both pressures were found to be significantly higher in the SNS group ($p<0.001$). Regarding rectal sensitivity, twenty-two studies reported on threshold, 21 on urge and 20 on maximum tolerable volumes. Outcomes were significant only for threshold volume ($p=0.03$). Decreases in urge volume and maximum tolerable volume did not reach statistical significance ($p=0.25$ and $p=0.48$, respectively). The most common complications among the 665 patients that underwent

permanent SNS implantation were pain or local discomfort (6%), lead displacement or breakage (4%), infection (3%) and sarcoma (3%). The authors noted that "the wide range of patients and consistently positive results in functional outcomes suggest that a placebo effect is unlikely; but further randomized controlled trials would be useful in confirming this." The authors also noted that SNS improves functional outcomes and quality of life in patients with fecal incontinence where conventional non-surgical therapies have failed.

Mowatt et al. (2008) performed a systematic review of three randomized studies involving a total of 38 patients. One study included 34 patients; each of the other studies included two patients. Thirty-one patients received sacral nerve stimulation (SNS). Two studies assessed the effects of SNS for fecal incontinence (n=36); one assessed the effects of SNS on constipation (n=2). All three studies had a double-blinded crossover design. According to the authors the very limited evidence suggests that for some selected patients, SNS can reduce episodes of fecal incontinence and urgency, and improve the ability to defer defecation, leading to a better quality of life. However, a minority may get worse despite apparently successful testing before permanent implantation.

Tjandra et al. (2008) published outcomes of the largest randomized controlled trial (RCT) to date involving 120 patients; 60 were randomized to the SNS group and 60 patients were randomized to best supportive therapy (i.e., pelvic floor exercises, bulking agents, dietary modifications, biofeedback). Fifty-four patients in the SNS group had ≥ 50% improvement in continence during the screening period with 53 patients undergoing SNS implantation. Follow-up was 12 months. Both groups were assessed at baseline, three, six, and 12 months.

The control group demonstrated no significant improvements in fecal continence as assessed by bowel diary, the Wexner score, and several quality-of-life scales. In the SNS group, mean incontinent episodes per week significantly improved at six and 12 months, as did mean incontinent days per week ($p<0.0001$ and 0.0001, respectively). Urge and passive incontinence also improved. Ability to defer defecation improved significantly but the ability to completely empty the bowel was not affected. One hundred percent fecal competence was achieved in 47.2% of patients. According to the authors, improvement in quality of life was noted immediately after implantation of the SNS, with significant improvement in all domains ($p<0.0001$). None of the patients had worsening of fecal incontinence as a result of SNS. There were no statistically significant changes in the maximum resting and squeeze anal canal pressures in either group. Adverse events in the SNS group included seroma (2%), pain at the implant site (6%) and tingling in the vaginal area (9%). In the control group six patients complained of constipation due to Imodium use. The authors noted that the presence of a control group helps reject the concept of a placebo effect. Data suggested that SNS may result in a decrease in the number incontinent episodes per week.

The Agency for Healthcare Research and Quality (Shamliyan, et al., 2007) reported results of a systematic review of several studies examining the effects of electrical stimulation or neuromodulation (i.e., SNS) on fecal incontinence. AHRQ noted that individualized sacral nerve continuous stimulation improved incontinence in 89% of patients with severe baseline incontinence compared to 17 percent after sham stimulation. However, the treatments did not improve quality of life with random differences after active and sham stimulation. All randomized controlled trials (RCTs) reported small inconsistent differences in anal manometry outcomes after active stimulation compared to the control. According to AHRQ electrical stimulation did not improve fecal incontinence in the majority of RCTs. "The significant relative improvement after sacral nerve stimulation in patients with severe baseline incontinence requires future confirmation in a large well designed RCT with long-term follow-up.

Regarding the use of self-report questionnaires to assess fecal incontinence, AHRQ also noted "Few validated questionnaires and instrumental methods were examined to detect the presence and baseline of causes for fecal incontinence with no consensus on which test is the gold standard. Patient reports do not correlate well with anatomical and physiological measures and anal manometry does not correlate well with ultrasonography or sigmoidoscopy. The severity and impact of incontinence on quality of life can be estimated from self-reported frequency, amount of leakage, and restrictions on daily activities, but not from instrumental methods. However, treatment decisions were made based on objective measures of incontinence. Instrumental physiological measurements that are associated with patient outcomes and may reflect better effects of different interventions should be analyzed in well-designed experiments."

Leroi et al. (2005) reported outcomes from a randomized double-blind crossover study involving 34 patients with fecal incontinence. Patients initially underwent peripheral nerve evaluation testing and if ≥ 50% improvement in incontinence was demonstrated they progressed to sacral nerve stimulation (SNS) implantation. All thirty-four patients received SNS; 27 patients were randomized to the crossover period, and 24 completed the study.

Outcomes measured were frequency of fecal incontinence and urgency episodes, delay in postponing defecation, score severity, feeling of improvement, preference for ON or OFF mode of stimulation, quality of life, and manometric measurements. Follow-up was 12 months. There was a significant treatment effect with a decrease in the median frequency of FI episodes between the ON and OFF periods; however, median incontinence episodes decreased in both the ON and OFF periods (90% versus 76%, respectively), as did defecation postponement (89% versus 63%, respectively). There was no significant change in the frequency of urgency episodes, the delay in postponing defecation, or the number of bowel movements per week between the periods of stimulation. There was improvement in the Cleveland Clinic incontinence score from baseline but no statistically significant difference between scores in the ON compared to the OFF periods. Additionally, there was no correlation between changes in the frequency of urgency episodes, delay in postponing defecation, Cleveland Clinic score, and changes in anal resting pressure, maximal squeeze pressure, squeeze pressure duration, threshold, constant sensation, and maximum tolerated volumes between the baseline and final periods. No significant change in the maximum anal resting pressure, squeeze pressure increment, and duration of voluntary contraction was noted between the two stimulation periods. Data suggested a treatment effect in regards to the frequency of episodes with the use of SNS. Additionally, improvement was noted in incontinence scores from baseline compared to periods of stimulation results.

Although randomized controlled trial data are limited prospective and retrospective data suggest that sacral nerve stimulation (SNS) may improve the number of incontinence episodes and quality of life measures as reported by study participants. It is noted the number of adverse events reported in some studies is not insignificant with infection rates of 6–10.8%, and stimulator removal rates of 12%. However, SNS is considered an acceptable treatment for selected individuals with fecal incontinence.

Other Indications
Less commonly SNS has been proposed for the treatment of various other conditions such as constipation and pelvic pain; however, data are limited and there is insufficient evidence in the peer-reviewed scientific literature to support safety and effectiveness (Maeda, et al., 2017, Pilkington, et al., 2017).

Literature Review - Sacral Nerve Stimulation for Other Indications: Zerbib et al. (2017) reported results of the CONSTIMOD (Efficacy of Sacral Nerve Modulation in Severe Refractory Constipation), a multicenter, randomized, double-blind, placebo-controlled, crossover study (n=36 patients). Adult patients were selected if they had chronic constipation for over one year defined

by at least two of the following criteria: two or fewer complete bowel movements per week; straining to evacuate at > 25% of attempts, or sensation of incomplete evacuation after defecation on > 25% of occasions. Other criteria for selection included absence of symptomatic response to standard therapies for at least three months. Exclusion criteria were constipation secondary to anorectal malformation, neurological disorders and/or opiates; previous colorectal surgery of any type; or significant pelvic floor anatomical abnormality (e.g., rectocele, rectal prolapse). Responders to an initial three-week peripheral nerve evaluation (n=20) were offered permanent implantation of a pulse generator and assigned randomly in a crossover design to two eight-week intervals of active or sham stimulation. At the end of the two trial periods, the patients received active stimulation until the final evaluation at one year. The primary outcome measured was the proportion of patients with a response during each treatment period (stimulation on and off). Response was measured over the last three weeks of each of the eight week treatment periods. Response to therapy was defined as at least three bowel movements per week and/or more than 50% improvement in symptoms. Secondary outcome measures included percentage of patients with a response at one year, effects of SNS on patients' daily bowel diary items, Wexner score, effect on QoL, visual analogue scale (VAS) score rating bowel habit, anorectal manometry parameters and colonic transit time. During the cross-over period, a positive response was observed in 12/20 and 11/20 patients after both active and sham stimulation periods, respectively ($p=0.746$). There was also no statistically significant difference between on and off periods for any item of the daily stool diary, Wexner score, VAS score, or QoL scores. At one year of follow-up, 16/20 patients were available for assessment; a total of 11 patients had a sustained clinical response. SNS was found to be associated with a significant improvement in QoL for symptoms ($p<0.001$), physical condition ($p=0.003$) and emotions ($p=0.004$). The mean difference in colonic transit times at baseline versus one-year follow-up was not found to be statistically significant ($p=0.226$). A total of nine serious adverse events occurred in eight patients, related to, pain, infection or dysfunction of the device. Study limitations included, small sample size and loss to follow-up. These study results did not support the use of SNS for refractory constipation.

A Cochrane review of randomized or quasi-randomized trials (n=8 studies) by Thaha et al. (2015) assessed the effectiveness of SNS using implanted electrodes for the treatment of fecal incontinence and constipation in adults. Of the eight trials, two cross over studies (n=61 patients) assessed SNS for constipation. Patient in both studies underwent permanent SNS implantation following a three-week trial of temporary stimulation. Outcomes measured in studies included frequency of stools and constipation symptoms, as well as quality of life. In the larger trial (Dinning, et al. 2015 [n=59 patients]), SNS did not improve frequency of bowel movements. Reported adverse effects (73) included pain at site of the implanted pulse generator (32), wound infection (12), and urological (17) events. The authors found limited evidence to suggest that SNS can improve fecal incontinence in a subset of patients. However, SNS was not found to improve symptoms in patients with constipation. Study results are limited by the number of studies and small sample sizes.

At present, the role of SNS for indications other than urinary urge incontinence, nonobstructive urinary retention, urinary urgency/frequency syndrome, and fecal incontinence has not been established.

Professional Societies/Organizations
American College of Gastroenterology (ACG): Wald et al. (2021) published guidelines regarding the management of benign anorectal disorders which included fecal incontinence. According to the ACG recommendations, "SNS can be recommended for patients with moderate to severe FI who have failed conservative measures, biofeedback, and other low-cost, low risk techniques". Grade of Recommendation: Strong recommendation based on low-quality evidence.

The guideline also mentioned that SNS has shown no benefit in treating constipation and cannot be recommended in patients with constipation of any type.

American College of Obstetricians and Gynecologists (ACOG)/American Urogynecologic Society (AUGS): The 2015 (reaffirmed 2022) joint ACOG/AUGS Practice Bulletin for urinary incontinence in women stated that sacral neuromodulation can be considered for patients with refractory urinary urge incontinence who have failed conservative treatment, including bladder training, pelvic floor physical therapy with biofeedback, and pharmacologic treatment.

American Society of Colon and Rectal Surgeons (ASCRS): In 2023, the ASCRS updated the clinical practice guideline for the management of fecal incontinence without a change in the previous recommendation. The ASCRS stated that SNS may be considered as a first-line surgical option for incontinent patients with and without sphincter defects. Grade of Recommendation: conditional recommendation based on low quality evidence (Bordeianou, et al., 2023)

The ASCRS clinical practice guideline for the evaluation and management of constipation stated that SNS may be an effective treatment for patients with chronic constipation and successful peripheral nerve evaluation test when conservative measures have failed; however, it is not currently approved by the US Food and Drug administration for this condition in the United States. Grade of Recommendation: Weak recommendation based on moderate quality evidence (Paquette, et al., 2016).

American Urological Association (AUA)/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU): The updated 2019 AUA/ SUFU guideline on the diagnosis and treatment of non-neurogenic overactive bladder in adults addressed sacral neuromodulation as a treatment option. The guideline stated that sacral neuromodulation may be offered as a third line treatment in a carefully selected patient population. For example, patients with severe refractory OAB symptoms or who are not candidates for second-line therapy and are willing to undergo a surgical procedure (Gormley, et al., 2012; Lightner, et al 2019 [updated]).

Percutaneous Tibial Nerve Stimulation (PTNS)

Overactive Bladder
The Urgent® PC Neuromodulation System (Uroplasty, Inc., Minneapolis, MN) is a minimally invasive neuromodulation system designed to deliver retrograde access to the sacral nerve through percutaneous electrical stimulation of the tibial nerve. It is performed in a physician office. The method of treatment is referred to as percutaneous tibial nerve stimulation (PTNS). The mechanism of action in neuromodulation of the bladder is not precisely understood, but neuromodulation likely interrupts abnormal reflex neurologic arcs, thus improving coordination of the detrusor and sphincter muscles. The majority of research in percutaneous tibial nerve stimulation (PTNS) has been for the treatment of overactive bladder (OAB) syndrome, defined as urinary urgency, usually accompanied by frequency and nocturia, with or without urgency urinary incontinence, in the absence of urinary tract infection or other obvious pathology (Haylen, et al., 2010). PTNS was developed as a less-invasive alternative to sacral nerve stimulation. A needle electrode is inserted at a depth of 3–4 cm near the tibial nerve at the medial malleolus. The needle is connected to a low-voltage, adjustable, hand-held stimulator, which sends an electrical impulse through the tibial nerve. The protocol for initial treatment typically consists of weekly 30-minute treatment sessions for 12 weeks. The protocol for maintenance PTNS treatment is less well defined, but will typically be done every three to four weeks after a beneficial response to the initial 12 week treatment (Kirby and Lentz, 2017).

U.S. Food and Drug Administration: Urgent® PC Neuromodulation System (Uroplasty, Inc., Minneapolis, MN) was FDA-approved October 2005. The Urgent PC Neuromodulation System

delivers PTNS and is intended to treat patients with overactive bladder and associated symptoms of urinary urgency, urinary frequency, and urge incontinence. In 2010 Urgent® PC Neuromodulation System (Uroplasty, Inc., Minnetonka, MN), received 510K approval as a substantially equivalent device with changes to the indication statement. The device is "intended to treat patients with overactive bladder (OAB) and associated symptoms of urinary urgency, urinary frequency, and urge incontinence". In 2015, Uroplasty Inc was merged into Cogentix Medical. In 2019, Cogentix was acquired by Laborie.

NURO Neuromodulation System was FDA-approved November 2013. The NURO Neuromodulation System is substantially equivalent to the Urgent PC Neuromodulation System and is "intended to treat patients with Overactive Bladder (QAB) and associated symptoms of urinary urgency, urinary frequency, and urge incontinence".

Literature Review - Percutaneous Tibial Nerve Stimulation (PTNS) for Overactive Bladder: PTNS has been evaluated primarily for overactive bladder syndrome in RCTs and systematic reviews/meta-analysis. There is sufficient evidence to support improved clinical outcomes using PTNS for the treatment of OAB and continued monthly maintenance therapy if there is a beneficial clinical response to the standard treatment regimen of 30-minute weekly sessions for 12 weeks (Salatzki, et al, 2019; Yoong, et al., 2013; Van der Pal, et al., 2006).

In a prospective cross-sectional cohort study Salatzki et al. (2019) assessed the factors influencing return for maintenance percutaneous tibial nerve stimulation (PTNS) treatment after successful completion of a 12-week course of PTNS treatment for overactive bladder (OAB). Included patients (n=83) experienced OAB symptoms and underwent 12 sessions of weekly PTNS treatment. Patients were evaluated at baseline and at week 12 using the International Consultation on Incontinence Questionnaire on OAB, the International Consultation on Incontinence Questionnaire on lower urinary tract symptom-related quality of life (ICIQLUTSqol) and a bladder diary (BD). Following treatment, patients (n=73) were placed into three groups: group 1 (n=25) did not respond to 12 weekly sessions of PTNS treatment; group 2 (n=17) responded to treatment but did not return for maintenance treatment and group 3 (n=31) responded to treatment and returned for maintenance treatment. Responders to treatment, evaluated using two patient-reported outcome measures, were invited to return for maintenance treatment when symptoms returned. The study measured factors influencing adherence to maintenance treatment after 12 sessions of PTNS treatment using a PTNS Service Evaluation Questionnaire. Patients belonging to groups 2 and 3 experienced a significant improvement from baseline to week 12 in total OAB scores ($p<0.05$). However, patients returning for maintenance treatment reported significant improvements specifically in nocturia (BD difference and ICIQ-LUTSqol difference, $p<0.05$, $p<0.05$, respectively) and perceived benefits of the treatment with regard to their OAB symptoms compared to those not returning for maintenance treatment (difference between the two groups 25.6%; $p=0.030$). Improvements in nocturia and perceived benefits predicted return for maintenance treatment based on a logistic regression analysis. Factors related to the need for repeat clinic visits, such as transportation, distance and time commitment, were not found to differ between the two groups. Author noted limitations included a small patient population, unbalanced subgroups and the results may not be reproducible in other healthcare models. The authors concluded that 12-session weekly PTNS is a safe and effective treatment for OAB. Responders to treatment returning for maintenance PTNS reported significant improvements in nocturia and perceived benefits over time, compared to those not returning for maintenance treatment.

Vecchioli-Scaldazza et al. (2018) performed a randomized controlled trial to assess effectiveness and durability of an antimuscarinic medication (group A) versus percutaneous tibial nerve stimulation (group B) versus combination therapy (group C) in women with overactive bladder syndrome (OAB). The study included women (n=105) with symptoms of overactive bladder

(urgency, urinary frequency, with or without urge incontinence). Patients were divided randomly into three groups of 35 patients each. Patients in Group A received antimuscarinic medication daily for 12 weeks. In Group B patients underwent PTNS once a week for 30 minutes each for a total of 12 weeks. In Group C patients underwent PTNS once a week for 30 minutes each for a total of eight weeks and antimuscarinic medication on alternate days also for eight weeks. The primary endpoint measured improvements in OAB symptoms, including daytime frequency, nighttime frequency, urgency and urge incontinence. The impact of OAB symptoms on patient's quality of life (QoL) and the patient impression of improvement were the measured secondary endpoints. A total of 27/35 patients completed the study. Combination therapy provided a clinically significant difference when compared to antimuscarinic medication in treating daily and nighttime micturition (p=0.0167). Combination therapy significantly reduces Urgency and urge incontinence compared to antimuscarinic medication and percutaneous tibial nerve stimulation (p=0.0005; p=0.0225 and p=0.0003; p=0.0015 respectively). Significant improvements in quality of life of patients (OAB-q SF, 6 and 13 items) were found after treatment in all groups evaluated. Adverse events were not reported. Author acknowledged limitations included the small patient population and the short-term follow-up of ten months. The study concluded that the combination of antimuscarinic medication and PTNS in the treatment of OAB symptoms was an effective and well-tolerated therapy with greater improvements and longer lasting effects than single treatments.

Vecchioli-Scaldazza et al. (2013) performed a randomized controlled crossover study (n=40) of women with OAB treated with PTNS or antimuscarinic medication. Exclusion criteria included stress incontinence, urinary tract infection, neurological disease, genital prolapse, uncontrolled narrow angle glaucoma, pelvic tumors or those previously treated with pelvic surgery, radiation therapy or antimuscarinic agents. Group A (n=20) received antimuscarinic medication daily for 40 days and underwent PTNS after three months from the end of therapy (i.e., washout period). PTNS treatment was given 30 minutes, twice a week for a total of six weeks. In group B (n=20), the women underwent PTNS as previously described and received antimuscarinic medication as above three months after the end of treatment. A total of 30/40 patients (75%) completed the study. The number of daily voids significantly decreased after each treatment compared to baseline. In group A, the mean number of daily voids pre- and post-medication differed significantly (medication p=0.004; PTNS <0.001). Similarly in group B, there was a statistically significant difference in pre- and post- treatment voids (medication p=0.008; PTNS <0.001). Secondary outcomes of nocturia, urge incontinence, and voided volume, also significantly improved after each treatment, with no significant differences between interventions. Study limitations included small sample size and loss to follow-up, however these short-term results suggest that PTNS is at least equivalent to antimuscarinic therapy for treating OAB symptoms.

Gungor et al. (2013) published results of an RCT (n=59) comparing transvaginal electrical stimulation (n=38) and PTNS (n=21) in women with OAB. Inclusion criteria were symptoms of OAB and detrusor overactivity. Exclusion criteria included pregnancy, cardiac disorders, neurological disorders, vesicoureteral reflux, menorrhagia, urinary tract infection or vaginitis, pelvic organ prolapse, and presence of an intrauterine device. The electrical stimulation protocol given to group one consisted of 20-minute treatments three times per week for six to eight weeks. PTNS was performed in group two with an Urgent PC device used for twelve 30-minute weekly sessions. A total of 52 of 59 (88%) patients completed the study. The groups did not differ significantly for outcomes of change in urgency, nocturia or incontinence episodes from baseline to the end of the treatment period. There was a statistically significant difference in daytime frequency (p=0.03). Study limitations included small sample size and participants lost to follow-up. Study results suggested that ES and PTNS may be equally effective in reducing symptoms of OAB.

An RCT by Peters et al. (2013) reported safety and efficacy results of PTNS for overactive bladder after three years of therapy. Patients (n=50) in the randomized, double-blind SUmiT (Sham

Effectiveness in Treatment of Overactive Bladder Symptoms) Trial who met the primary effectiveness end point after 12 weekly percutaneous tibial nerve stimulation treatments were enrolled in this prospective study to assess long-term outcomes. Subjects in this STEP (Sustained Therapeutic Effects of Percutaneous Tibial Nerve Stimulation) Study were prescribed a fixed schedule 14-week tapering protocol followed by an individual treatment plan aimed at sustaining overactive bladder symptom improvement. A total of 29 patients completed the 36-month protocol. Statistical analysis estimated that 77% of patients maintained moderate or marked improvement in overactive bladder symptoms at three-year follow-up. Compared to baseline, the frequency of median voids per day, urge incontinence episodes, and nighttime voids, decreased significantly (all $p<0.0001$). All quality-of-life parameters remained markedly improved from baseline through three years ($p<0.0001$). Limitations of this study include the small patient population and loss to follow-up. The authors concluded that most patients with an initial positive response to 12 weekly percutaneous tibial nerve stimulation treatments safely sustained overactive bladder symptom improvement to three years with an average of one treatment per month.

The Agency for Healthcare Research and Quality (AHRQ) published a 2012 comparative effectiveness review of nonsurgical treatments for urinary incontinence in adult women. The clinical effects of PTNS were examined in four RCTs that compared PTNS and no active treatment in patients with OAB. The longest follow-up time period was 12 weeks. The AHRQ report provided a pooled analysis of data from three studies (n=405 patients) that found statistically significantly greater improvement in urinary incontinence in the PTNS compared to control group (RR: 1.9, 95% CI: 1.1 to 3.2). Evidence from one study was insufficient to conclude better effectiveness of PTNS compared to medication. No RCTs compared continence after PTNS versus sham stimulation beyond 12 weeks. Evidence from one study was insufficient to conclude better effectiveness of PTNS compared to medication. The study results indicated that PTNS improved urinary incontinence compared to sham treatment in the short-term (Shamliyan et al., 2012).

A systematic review and meta-analysis (n=16 studies/940 subjects) by Burton et al. (2012) evaluated the effectiveness of posterior PTNS in treating overactive bladder symptoms. Studies included RCTs (n=6), and prospective, non-comparative studies (n=10). PTNS was compared to sham in four RCTs showing a significant difference favoring PTNS [RR 7.02 95% confidence interval (CI) 1.69-29.17]. PTNS was compared to anticholinergic medication in two RCTs with no significant difference in the change in bladder diary parameters between the treatments. The pooled subjective success rate was 61.4% (95% CI 57.5-71.8) and objective success rate was 60.6% (95% CI 49.2-74.7). Although there was evidence of significant improvement in overactive bladder symptoms comparable to the effect of anticholinergic medication, the studies included in the review only considered short-term outcomes after initial treatment. The review summarized that in order to recommend PTNS as a practical treatment option, long-term data and health economic analysis are needed.

Monga et al. (2012) performed a systematic review of the evidence for a range of electrical stimulation therapies in the treatment of lower urinary tract symptoms. Of the 72 studies reviewed, a total of 16 evaluated PTNS. These included prospective case series (n=13) and randomized comparative studies (n=3). Findings indicated that median mean reductions in incontinence episodes and voiding frequency were similar for implanted SNS and PTNS, with median mean values of 72 and 66% for incontinence episodes and median mean values of 40 and 32.5% for voiding frequency for SNS and PTNS, respectively. However, it was determined that additional long-term follow-up studies are needed to validate the ability of this therapy to produce sustained benefit (Monga, et al., 2012). Additional systematic reviews without meta-analysis (Moossdorff-Steinhauser, et al., 2013; Gaziev, et al., 2013; Biemans, et al., 2013; Levin, et al., 2012) included the same RCTs and draw similar conclusions that limited high quality data

demonstrated that PTNS is an effective and safe option to treat OAB patients, but further studies are needed to assess the long-term durability of the treatment.

Peters et al. (2010) conducted a RCT comparing the efficacy of PTNS to sham through 12 weeks of therapy. The eligibility criteria included a score of at least four on the overactive bladder questionnaire (OAB-q) short form for urgency, self-reported bladder symptoms lasting at least three months, and failure of conservative management. A total of 220 patients were randomized, 110 to the PTNS group and 110 to the sham group. Females accounted for 86 (78.2%) of the PTNS subjects and 88 (80.0%) of the sham subjects. The sham group underwent stimulation through a TENS unit with no needle insertion. Both groups received 12 weekly 30-minute intervention sessions. The 12-week course of treatment was completed by 103 of 110 (94%) in the PTNS group and 105 of 110 (95%) in the sham group. Global response assessment (GRA) at 13 weeks compared to baseline for overall bladder symptoms improvement demonstrated 60/103 (58.3%) for PTNS and 23/105 (21.9%) for sham ($p<0.001$). This is statistically significant. In total, six PTNS subjects reported nine mild or moderate treatment related adverse events consisting of ankle bruising (1 of 110, 0.9%), discomfort at the needle site (2 of 110, 1.8%), bleeding at the needle site (3 of 110, 2.7%) and tingling in the leg (1 of 110, 0.9%). No local treatment related adverse events were reported in the sham group. In addition, no systemic adverse events were experienced in either group. The authors concluded that PTNS therapy is safe and effective in treating OAB symptoms. Limitations of the SUmiT trial included the primary outcome measured used was a single response, patient-reported global response assessment (GRA) and there was short follow-up of three months.

Finazzi-Agro et al. (2010) also performed a RCT comparing PTNS with a sham. A total of 35 female patients presenting with detrusor overactivity incontinence that did not respond to anti-muscarinic therapy were randomly assigned to percutaneous tibial nerve stimulation or to a control group. The percutaneous tibial nerve stimulation group (18 patients) was treated with 12 percutaneous tibial nerve stimulation sessions. The control group (17 patients) received an original placebo treatment using a 34-gauge needle placed in the medial part of the gastrocnemius muscle. Patients showing a reduction in urge incontinence episodes greater than 50% were considered responders. PTNS was performed three times per week for four weeks. The primary outcome for this study was the percent responders, defined as a greater than 50% reduction in incontinent episodes. This endpoint was reached by 71% (12/17) of patients in the PTNS group, compared with 0% (0/15) in the placebo group ($p<0.001$). No serious side effects were reported in either group but patients in both groups reported occasional transient pain at the stimulation site. Study limitations included small patient population and short follow-up.

In an RCT, Peters et al. (2009) compared the effectiveness of a series of 12 weekly, 30-minute office based PTNS treatments and 12 weeks of 4 mg daily extended-release tolterodine tartrate (Detrol® LA). Included were ambulatory adults with overactive bladder (OAB) symptoms, with or without a history of previous anticholinergic drug use, with at least eight voids per 24 hours documented by history and physical and voiding diary. Females made up 90% of the participants. Of the patients who completed 12 weeks of therapy, 41 of 44 receiving PTNS and 43 of 43 on tolterodine completed the voiding diary. Using the Global Response Assessment (GRA), subject assessment of OAB symptom improvement compared to baseline was dramatically greater in the PTNS arm with 79.5% reporting cure or improvement compared to 54.8% of subjects on tolterodine ($p=0.01$). This global assessment of improvement may have been greater because subjects in the PTNS arm may have had less significant side effects or more perceived improvement in subjective changes such as urgency, or because of the novel nature of the treatment. Limitations of this study included: industry-sponsored; no sham/placebo control group; potential for observation bias (PTNS group assessed in-person, tolterodine group assessed by phone). After 12 weeks, subjects randomized to weekly PTNS were offered an additional nine months of treatment with assessments at six and 12 months from baseline (MacDiarmid, et al.,

2010). A total of 33 PTNS responders continued therapy with 32 and 25 subjects completing six and 12 months of therapy, respectively. Subjects received a mean of 12.1 treatments during an average of 263 days, with a median of 17 days between treatments. At six months 94% of subjects classified OAB symptoms as improved from baseline and 96% reported improvement at 12 months. Overactive bladder questionnaire symptom severity was significantly improved from 12 weeks to 12 months ($p<0.01$) as well as from six to 12 months ($p<0.01$). No serious adverse events occurred. Limitations included: no control group; the definition of response used was not standardized and based entirely on a GRA; there was not a standardized treatment protocol as patients returned for maintenance therapy at irregular intervals as dictated by patient preference. There is sufficient evidence in the peer-reviewed scientific literature to support the short-term safety and efficacy of PTNS as a treatment for OAB symptoms.

Implantable Tibial Nerve Stimulation

There are several implantable tibial nerve stimulation devices (eCoin®, RENOVA™ iStim system, Bioness StimRouter System) that are being studied for the treatment of urinary tract dysfunction (e.g., overactive bladder, urinary urge incontinence).

These devices are surgically implanted in the posterior tibial nerve area and stimulated externally. The eCoin, a miniaturized leadless neurostimulator was recently approved by the FDA. The eCoin is inserted near the ankle, above the tibial nerve using only local anesthetic and is proposed to provide automatic, intermittent tibial nerve stimulation to reduce urge urinary incontinence without patient remote management (Valencia Technologies, Inc, 2022).

U.S. Food and Drug Administration: According to the FDA, eCoin® Peripheral Neurostimulator (Valencia Technologies Corporation, CA) received premarket approval (PMA) on July 15, 2022. Per the FDA the eCoin® Peripheral Neurostimulator "is indicated to treat urgency urinary incontinence in patients intolerant to or having an inadequate response to other more conservative treatments or who have undergone a successful trial of percutaneous tibial nerve stimulation." According to the FDA summary of safety and effectiveness data (SSED), two post-approval studies (PAS) are required. The first is continued follow-up of the "Pivotal Study of Subcutaneous Tibial Nerve Stimulation with eCoin® for OAB with Urinary Urge Incontinence" and report clinical outcomes, including all device-or procedure-related adverse events to FDA through five years post-implantation. The second is a prospective, single-arm, multi-center, observational study designed to collect effectiveness and safety data in a post-approval setting. Effectiveness will be determined at 12 and 24 months and continue to be collected for five years post-implantation of study subjects (FDA, 2022)

Literature Review: The overall body of literature reports that there is insufficient evidence to draw conclusions regarding the effectiveness of implantable tibial nerve stimulation for the treatment of urinary voiding dysfunction, fecal incontinence and constipation. Studies are of low quality with small patient populations and short-term follow-ups (Kaaki, et al., 2022; Gilling, et al., 2021; Rogers, et al., 2021; Dorsthorst, et al., 2020).

Rogers et al. (2021) conducted a prospective, open-label, single arm trial that evaluated the safety and efficacy of the eCoin® for the treatment of refractory urgency urinary incontinence (UUI). Adults aged 18–80 with daily UUI who were intolerant or had an inadequate response to, at least one second or third-line therapy prior to enrollment were included in the study. One-hundred thirty-seven patients had the eCoin implanted subcutaneously using only local anesthetic in the medial lower leg above the fascia. Four weeks after implantation with minimal swelling confirmed, the device was activated. The eCoin delivered automated stimulation sessions for the duration of the study. Automated stimulation sessions occur for 30-minute durations every three days for 18 weeks and every four days thereafter. The primary outcomes measured the efficacy and safety of

the device. Efficacy was measured by the proportion of patients who achieved a 50% or greater reduction from baseline in urgency urinary incontinence episodes after 48 weeks of therapy. Safety outcome measured device-related adverse events at the same time point. After activation, patients had follow-up visits at four, eight, 12, 24, 36 and 48 weeks. At each follow-up, a 3-day voiding diary was collected and the OAB Questionnaire, Patient Global Impression of Improvement, and a custom Likert scale on subject satisfaction questionnaires were administered. Patients were questioned about adverse events, initiation of OAB medications, any other changes to their history or comments regarding the device. Reprogramming was offered at the eight, 24 and 36-week visits. At 48 weeks post-activation, participants replied to a non-validated questionnaire detailing their experience with the device, implant procedure and their attitudes towards eCoin compared to other therapies. The primary efficacy analysis showed 68% of the intention to treat population (n=132) experienced at least a 50% reduction in urgency urinary incontinence episodes at 48 weeks post-activation; 16% of implanted subjects experienced device-related events through 52 weeks post-implantation. Author noted limitations included the lack of blinding and comparison along with the short-term follow-up. The authors concluded that eCoin demonstrated clinical benefit for treating overactive bladder syndrome with automatic delivery of an intermittent low-duty cycle and implanted with a minimally invasive, brief procedure. Additional long term randomized control trials with large patient populations are needed to validate the outcomes of the study. No health disparities were identified by the investigators.

Professional Societies/Organizations
American Society of Colon and Rectal Surgeons (ASCRS): In 2023, the ASCRS updated the clinical practice guideline for the management of fecal incontinence. The ASCRS stated that "treatments for FI that are not currently approved for use in the United States by the Food and Drug Administration (FDA), have become unavailable in the United States, or lack clinical data to support their use are beyond the scope of this guideline" (Bordeianou, et al., 2023).

American Urological Association (AUA)/Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU): The AUA/SUFU guideline on the diagnosis and treatment of non-neurogenic OAB in adults addressed using PTNS as a treatment option. The guideline stated that clinicians may offer PTNS as third-line treatment in a carefully selected patient population, characterized by moderately severe baseline incontinence and frequency and willingness to comply with the PTNS protocol. Additionally, the guidelines stated that patients must also have the resources to make frequent office visits both during the initial treatment phase and to obtain maintenance treatments in order to achieve and maintain treatment effects. This determination was based on evidence the AUA categorized as Grade C because of the primarily observational designs, varying patient inclusion criteria and short follow-up in most studies (Gormley, et al., 2012; Lightner, et al 2019 [updated]).

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	Sacral Nerve Stimulation For Urinary Incontinence (230.18)	1/01/2002
LCD	National Government Services, Inc.	Posterior Tibial Nerve Stimulation for Voiding Dysfunction (L33396)	10/24/2019

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

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

Sacral Nerve Stimulation (SNS)

Considered Medically Necessary as a screening trial for sacral nerve stimulation (SNS) when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
64561	Percutaneous implantation of neurostimulator electrode array; sacral nerve (transforaminal placement) including image guidance, if performed
64581	Open implantation of neurostimulator electrode array; sacral nerve (transforaminal placement)

HCPCS Codes	Description
C1778	Lead, neurostimulator (implantable)
C1897	Lead, neurostimulator test kit (implantable)

Considered Medically Necessary for permanent SNS implantation when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
64581	Open implantation of neurostimulator electrode array; sacral nerve (transforaminal placement)
64585	Revision or removal of peripheral neurostimulator electrode array
64590	Insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling
64595	Revision or removal of peripheral or gastric neurostimulator pulse generator or receiver

HCPCS Codes	Description
A4290	Sacral nerve stimulation test lead, each
C1767	Generator, neurostimulator (implantable), non-rechargeable
C1778	Lead, neurostimulator (implantable)
C1787	Patient programmer, neurostimulator
C1820	Generator, neurostimulator (implantable), with rechargeable battery and charging system
C1883	Adaptor/extension, pacing lead or neurostimulator lead (implantable)
L8679	Implantable neurostimulator, pulse generator, any type
L8680	Implantable neurostimulator electrode, each
L8681	Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
L8682	Implantable neurostimulator radiofrequency receiver

HCPCS Codes	Description
L8685	Implantable neurostimulator pulse generator, single array, rechargeable, includes extension
L8686	Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension
L8687	Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
L8688	Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension

Percutaneous Tibial Nerve Stimulation (PTNS)

Considered Medically Necessary when used to report PTNS treatment of overactive bladder symptoms when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
64566	Posterior tibial neurostimulation, percutaneous needle electrode, single treatment, includes programming

Considered Experimental/Investigational/Unproven when used to report Implantable tibial nerve stimulation for the treatment of urinary voiding dysfunction (e.g., overactive bladder, urinary urge incontinence), fecal incontinence and constipation:

CPT®* Codes	Description
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 (eg, 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 (eg, 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

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Revision Details

Type of Revision	Summary of Changes	Date
Annual review	• Updated to new template and formatting standards. • Removed policy statement for PTNS maintenance therapy and number of treatments allowed. • Removed EIU policy statement for PTNS for fecal incontinence and constipation.	10/15/2023