BlueCross BlueShield
of Alabama

Name of Policy:

Sacral Nerve Modulation/Stimulation for Pelvic Floor Dysfunction

Policy #: 159 Latest Review Date: April 2018
Category: Surgery Policy Grade: A

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

Sacral nerve stimulation (SNS), also referred to as sacral nerve neuromodulation (SNM), is defined as the implantation of a permanent device that modulates the neural pathways controlling bladder or rectal function. This policy addresses the use of SNS in the treatment of urinary or fecal incontinence, urinary or fecal nonobstructive retention, or chronic pelvic pain in patients with intact neural innervation of the bladder and/or rectum.

Urinary and Fecal Incontinence

Urge incontinence is defined as leakage of urine when there is a strong urge to void. Urgency-frequency is an uncontrollable urge to urinate, resulting in very frequent, small volumes and is a prominent symptom of interstitial cystitis. Urinary retention is the inability to completely empty the bladder of urine. Fecal incontinence can arise from a variety of mechanisms, including rectal wall compliance, efferent and afferent neural pathways, central and peripheral nervous systems, and voluntary and involuntary muscles. Fecal incontinence is more common in women, due mainly to muscular and neural damage that may occur during vaginal delivery.

Treatment

Treatment using sacral nerve neuromodulation, also known as indirect sacral nerve stimulation, is one of several alternative modalities for patients with urinary or fecal incontinence (urge incontinence, significant symptoms of urgency-frequency, nonobstructive urinary retention) who have failed behavioral (e.g. prompted voiding) and /or pharmacologic therapies.

The sacral nerve neuromodulation device consists of an implantable pulse generator that delivers controlled electrical impulses. This pulse generator is attached to wire leads that connect to the sacral nerves, most commonly the S3 nerve root. Two external components of the system help control the electrical stimulation. A control magnet is kept by the patient and can be used to turn the device on or off. A console programmer is kept by the physician and used to adjust the settings of the pulse generator.

Prior to implantation of the permanent device, patients undergo an initial testing phase to estimate potential response to treatment. The first type of testing developed was percutaneous nerve evaluation (PNE). This procedure is done with the patient under local anesthesia, using a test needle to identify the appropriate sacral nerve(s). Once identified, a temporary wire lead is inserted through the test needle and left in place for several days. This lead is connected to an external stimulator, which is carried by patients in their pocket or on their belt. Patients then keep track of voiding symptoms while the temporary device is functioning. The results of this test phase are used to determine whether patients are appropriate candidates for the permanent device. If patients show a 50% or greater reduction in incontinence frequency, they are deemed eligible for the permanent device.

The second type of testing is a 2-stage surgical procedure. In the first stage, a quadripolar-tined lead is implanted (Stage 1). The testing phase can last as long as several weeks, and if patients show a 50% or greater reduction in symptom frequency, they can proceed to Stage 2 of the surgery, which is permanent implantation of the neuromodulation device. The 2-stage surgical procedure has been used in various ways. These include its use instead of PNE, for patients who failed PNE, for patients with an inconclusive PNE, or for patients who had a successful PNE to further refine patient selection.

The permanent device is implanted with the patient under general anesthesia. An incision is made over the lower back, and the electrical leads are placed in contact with the sacral nerve root(s). The wire leads are extended through a second incision underneath the skin, across the flank to the lower abdomen. Finally, a third incision is made in the lower abdomen where the pulse generator is inserted and connected to the wire leads. Following implantation, the physician programs the pulse generator to the optimal settings for that patient. The patient can switch the pulse generator between on and off by placing the control magnet over the area of the pulse generator for 1–2 seconds.

This evidence review does not address pelvic floor stimulation, which refers to electrical stimulation of the pudendal nerve. Pelvic floor stimulation is addressed separately (*see Medical Policy #201 Pelvic Floor Stimulation as a Treatment of Urinary and Fecal Incontinence*).

Policy:

Effective for dates of service on or after September 4, 2015:

A trial period of sacral nerve neuromodulation with either percutaneous nerve stimulation or a temporarily implanted lead meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage in patients with **urinary incontinence and nonobstructive retention** who meet **all** of the following criteria:

1. There is a diagnosis of at least one of the following:
    a. Urge incontinence
    b. Urgency-frequency syndrome
    c. Non-obstructive urinary retention
    d. Overactive bladder
2. There is documented failure or intolerance to conventional conservative therapies (e.g., behavioral training such as bladder training, prompted voiding, or pelvic muscle exercise training, pharmacologic treatment for at least a sufficient duration to fully assess its efficacy, and/or surgical corrective therapy).
3. The patient is an appropriate surgical candidate.
4. Incontinence is not related to a neurologic condition.

Permanent implantation of a sacral nerve neuromodulation device meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage in patients with **urinary incontinence and nonobstructive retention** who meet **all** of the following criteria:

1. All of the criteria above (trial period 1-4) are met.
2. A trial stimulation period demonstrates at least 50% improvement in symptoms over a period of at least 48 hours.

Other urinary/voiding applications of sacral nerve neuromodulation do not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage, **including but not limited** to treatment of stress incontinence or urge incontinence due to a neurologic condition, e.g., detrusor hyperreflexia, multiple sclerosis, spinal cord injury, or other types of chronic voiding dysfunction, Blue Cross and Blue Shield of Alabama's medical criteria for coverage and are considered **investigational**.

A trial period of sacral nerve neuromodulation with either percutaneous nerve stimulation or a temporarily implanted lead meets Blue Cross and Blue Shield's medical criteria for coverage in patients with **fecal incontinence** who meets **all** of the following criteria:

1. There is a diagnosis of chronic fecal incontinence of greater than two incontinent episodes on average per week with duration greater than six months or for more than 12 months after vaginal childbirth.
2. There is documented failure or intolerance to conventional conservative therapy (e.g., dietary modification, the addition of bulking and pharmacologic treatment) for at least a sufficient duration to fully assess its efficacy.
3. The patient is an appropriate surgical candidate.
4. The condition is not related to an anorectal malformation (e.g., congenital anorectal malformation; defects of the external anal sphincter over 60 degrees; visible sequelae of pelvic radiation; active anal abscesses and fistulae) or chronic inflammatory bowel disease.
5. Incontinence is not related to a neurologic condition.
6. The patient has not had rectal surgery in the previous 12 months, or in the case of cancer, the patient has not had rectal surgery in the past 24 months.

Permanent implantation of a sacral nerve neuromodulation device meets Blue Cross and Blue Shield's medical criteria for coverage in patients with **fecal incontinence** who meets **all** of the following criteria:

1. All of the criteria above (trial period 1-6) are met.
2. A trial stimulation period demonstrates at least 50% improvement in symptoms over a period of at least 48 hours.

Sacral nerve neuromodulation does not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage for the treatment of chronic constipation or chronic pelvic pain and is considered **investigational.**

<u>Effective for dates of service on or after September 9, 2014 and prior to September 4, 2015:</u>
Sacral nerve neuromodulation meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage for the **treatment of urge incontinence, urgency-frequency syndrome, non-obstructive urinary retention and overactive bladder in patients when all of the following criteria are met:**

- Documented failure or intolerance to conventional conservative therapy (e.g., behavioral training such as bladder training, prompted voiding, or pelvic muscle exercise training, pharmacologic treatment for at least a sufficient duration to fully assess its efficacy, and/or surgical corrective therapy); AND
- The patient is an appropriate surgical candidate; AND

- A successful percutaneous test stimulation, defined as at least 50% improvement in symptoms over a period of at least one week **(effective on or after April 11, 2013)**, was performed; AND
- Condition is not related to a neurologic condition.

Sacral nerve neuromodulation meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage for the **treatment of fecal incontinence when all of the following criteria are met:**

- Chronic fecal incontinence of greater than two incontinent episodes on average per week with duration greater than six months or for more than 12 months after vaginal childbirth; AND
- Documented failure or intolerance to conventional conservative therapy (e.g., dietary modification, the addition of bulking and pharmacologic treatment for at least a sufficient duration to fully assess its efficacy, performed more than 12 months [or 24 months in case of cancer] previously); AND
- The patient is an appropriate surgical candidate; AND
- A successful percutaneous test stimulation, defined as at least 50% improvement in symptoms over a period of at least two weeks, was performed; AND
- Condition is not related to an anorectal malformation (e.g., congenital anorectal malformation; defects of the external anal sphincter over 60 degrees; visible sequelae of pelvic radiation; active anal abscesses and fistulae) or chronic inflammatory bowel disease; AND
- Incontinence is not related to another neurologic condition such as peripheral neuropathy or complete spinal cord injury.

Temporary or permanent sacral nerve neuromodulation/stimulation does not meet Blue Cross and Blue Shield of Alabama's medical criteria for **treatment of chronic voiding dysfunction or treatment of fecal incontinence** not described above, including, but not limited to, stress incontinence or urge incontinence due to neurologic conditions (e.g., detrusor hyperreflexia, multiple sclerosis, diabetic neuropathy or spinal cord injury), chronic constipation or chronic pelvic pain.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

The literature has been periodically updated using the MEDLINE database. The most recent literature review was performed through February 05, 2018.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function-including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Urinary Incontinence

Randomized Controlled Trials

Several randomized controlled trials (RCTs) on SNM for urinary incontinence have been conducted. The first study was sponsored by Medtronic and submitted to the U.S. Food and Drug Administration as part of the approval process. Findings have not otherwise been published. Based on this RCT, the 1998 TEC Assessment concluded that SNM reduced urge incontinence compared with control patients. This well-designed trial, using standardized clinical and functional status outcomes measurements, enrolled patients with severe urge incontinence who had failed extensive prior treatments. The magnitude of effect (approximately one-half of the patients became dry, three-quarters experienced at least 50% reduction in incontinence) was fairly large, probably at least as great as with surgical procedures, and larger than expected from a placebo effect or from conservative measures such as behavioral therapy or drugs. The therapy evaluation test, in which the device is turned off (i.e., sham treatment is provided) and patients thus serve as their own controls, provided further evidence that the effect on incontinence is due to electrical stimulation and demonstrates that the effect of SNM is reversible. The cohort analysis of the clinical trial provides some evidence that the effect of SNM is maintained for up to 2 years. There was a high rate of adverse events reported in this clinical trial. Most of the adverse events were minor and reversible; however, approximately one-third of patients required surgical revision for pain at the operative sites or migration of the leads.

In this RCT, 177 of 581 patients had urinary retention. Patients with urinary retention reported significant improvements in terms of volume catheterized per catheterization, a decrease in the number of catheterizations per day, and increased total voided volume per day. At 12 months postimplant, 61% of patients had eliminated the use of catheterization. A total of 220 of 581 (38%) had significant urgency-frequency symptoms. After 6 months, 83% of patients with urgency-frequency symptoms reported increased voiding volumes with the same or reduced degree of frequency. At 12 months, 81% of patients had reached normal voiding frequency. Compared with a control group, patients with implants reported significant improvements in quality of life (QOL), as evaluated by the Short-Form 36-Item Health Survey.

An additional prospective RCT of 44 patients with urge incontinence was published in 2000. At 6 months, the implant group showed significantly greater improvement on standardized clinical outcomes, compared with those receiving conservative therapy. The magnitude of effect was substantial.

Siegel et al (2015) published results of an industry-sponsored FDA-mandated postapproval study and are known as the Insite trial. This study compared SNM using a two-stage surgical procedure to standard medical therapy. Study inclusion criteria included a diagnosis of overactive bladder (at least 8 voids per day and/or at least 2 involuntary leaking episodes in 72 hours) and a failed trial of at least one anticholinergic or antimuscarinic medication. In addition, there needed to be at least 1 such medication that had not yet been attempted. Patients with neurologic diseases and with primary stress incontinence were excluded. A total of 70 patients were allocated to SNM and 77 to standard medical therapy. Of the 70 patients in the SNM group, 11 elected not to receive test stimulation with the tined lead and eight received the lead but did not receive a full system implant due to lack of response to a 14-day test stimulation period (response was defined as at least a 50% reduction in average leaks and/or voids). Patients in the medical treatment group tried the next recommended medication or restarted a discontinued medication. Therapeutic success was defined as at least a 50% improvement in average leaks/day or at least a 50% improvement in the number of voids per day or a return to fewer than 8 voids per day. In an intention-to-treat analysis, the therapeutic success rate at 6 months was 61% in the SNM group and 42% in the standard medical treatment group; the difference between groups was statistically significant (p=0.02). QOL at six months was a secondary outcome. Several validated QOL scales were used, and all favored the SNM group compared with the standard medical treatment group (p<0.002 for all comparisons).

Twelve-month follow-up of the Insite trial were published by Noblett et al in 2014. The analysis included patients included in the SNS group of initial RCT plus additional patients enrolled and implanted in the interim. A total of 340 patients underwent test stimulation, 272 underwent implantation, and 255 completed 12 months of follow-up. In a modified completers' analysis, the therapeutic success rate was 82%. This modified completers' analysis included patients who were implanted and had either a baseline or 12-month evaluation, or withdrew from the trial due to a device-related adverse event or lack of efficacy. In an analysis limited to study completers, the therapeutic response rate was 85%. The Noblett analysis did not include data from the control group of patients receiving only standard medical therapy.

In 2016, Amundsen et al reported on a RCT comparing intradetrusor injection of onabotulinumtoxinA (n=192) with SNM (n=189) in women with refractory urgency urinary incontinence, defined least 1 supervised behavioral or physical therapy intervention and the use of a minimum of 2 anticholinergics (or inability to tolerate or contraindications to the medication). In intention-to-treat analysis, patients in onabotulinumtoxinA-treated patients had greater reductions in urge incontinence per day in SNM-treated patients: 3.9 vs 3.3/ day (mean difference: 0.63; 95% CI 0.13 to 1.14, P=0.01). OnabotulinumtoxinA -treated patients had greater reductions in some overactive bladder-related quality of life questionnaire-related measures, although the clinical meaningfulness of the changes was uncertain. Patients in the onabotulinumtoxinA-treated group were more likely to have urinary tract infections (UTIs, 35% vs 11%; risk difference -23%, 95% CI -33% to -13%, P<0.001).

Case Series
In addition to the RCTs, case series have been published in recent years and some had longer follow-up than the RCTs. For example, a 2011 series by Groen et al in the Netherlands reported the longest follow-up. A total of 60 patients had at least 5 years of follow-up after SNM for refractory idiopathic urge urinary incontinence. Success was defined as at least a 50% decrease in the number of incontinent episodes or pads used per day. The success rate was 52 of 60 (87%) at one month and gradually decreased to 37 (62%) at five years. The number of women who were completely continent was 15 (25%) at one month and nine (15%) at 5 years. At the 5-year follow-up, SNM was still used by 48/60 (80%) women. A total of 57 adverse events were reported in 32 of 60 (53%) patients. The most frequent adverse events were hardware-related or pain or discomfort. There were a total of 23 reoperations in 15 patients. In most cases, pain problems were managed conservatively.

Findings from a large prospective series were reported in 2009 by White et al. The study focused on complications associated with SNM in 202 patients with urge incontinence, urinary urgency, or urinary retention. At a mean follow-up of 37 months (range, 7 to 84), 67 patients (30%) had experienced adverse events that required either lead or implantable pulse generator revisions. Complications included pain (3%), device malfunction secondary to trauma (9%), infection (4%), postoperative hematoma (2%), and lead migration (6%). In addition, 5% of patients underwent elective removal, 4% had device removal due to lack of efficacy, and 2% required removal due to battery expiration. At the last follow-up, 172 patients (85%) had functional implanted units.

Section Summary: Urinary Incontinence
Data from RCTs and case series with long-term follow-up suggest that SNM reduces symptoms of urge incontinence, urgency-frequency syndrome, nonobstructive urinary retention and overactive bladder in selected patients.

Fecal Incontinence
Thaha et al (2015) published a Cochrane review on sacral nerve stimulation for fecal incontinence and constipation in adults, which included randomized, quasi-randomized, and crossover trials. For fecal incontinence, the review included 6 trials of SNM (n=219), 2 of which used a parallel group design (Thin et al [2015], Tjandra et al [2008]) and the remaining of which used a crossover design. The primary methodological quality issue noted was related

to lack of clarity around randomization techniques and allocation concealment. The review concluded, “The limited evidence from the included trials suggests that SNS can improve continence in a proportion of patients with faecal incontinence.”

Thin et al (2013) published a systematic review of randomized trials and observational studies on SNM for treating fecal incontinence. A total of 61 studies met eligibility criteria; including at least ten patients, having a clear follow-up interval and reporting the success rate of therapy based on a 50% or greater improvement in fecal incontinence episodes. Only two of the studies were RCTs (the Tjandra et al and Leroi et al studies, described next) and 50 were prospective case series. Data from two studies with long-term follow-up could be pooled to calculate median success rates using an intention-to-treat analysis. These median success rates were 63% in the short term (no more than 12 months’ follow-up), 58% in the medium term (12-36 months), and 54% in the long term (>36 months). The per-protocol short-, medium-, and long-term success rates were 79%, 80%, and 84%, respectively.

Previously, in 2011, Tan et al published a meta-analysis of studies SNM for treating fecal incontinence. They identified a total of 34 studies that reported on at least one of their outcomes of interest and clearly documented how many patients underwent temporary and permanent SNM. Only one of these studies was an RCT (Tjandra et al). In the 34 studies, a total of 944 patients underwent temporary sacral nerve stimulation (SNS) and 665 subsequently underwent permanent SNS implantation. There were 279 patients who did not receive permanent implantation, and 154 of these were lost to follow-up. Follow-up in the studies ranged from two weeks to 35 weeks. In a pooled analysis of findings of 28 studies, there was a statistically significant decrease in incontinence episodes per week with SNM compared with maximal conservative therapy (weighted mean difference, -6.83; 95% confidence interval [CI], -8.05 to -5.60; $p<0.001$). Fourteen studies reported incontinence scores, and when these results were pooled, there was also a significantly greater improvement in scores with SNS compared with conservative therapy (weighted mean difference, -10.57; 95% CI, -11.89 to -9.24; $p<0.001$).

<u>Randomized Controlled Trials</u>
In 2008, Tjandra et al published an RCT with 120 patients with severe fecal incontinence. Patients were randomly assigned to receive SNS or best supportive therapy, consisting of pelvic floor exercises with biofeedback, bulking agents, and dietary management with a team of dieticians. Exclusion criteria included neurologic disorders and external anal sphincter defects of more than 120 degrees of the circumference, although a “high proportion” of the patients had pudendal neuropathy. The study was not blinded. Of the 60 patients randomized to SNS, 54 (90%) had successful test stimulation and 53 decided to proceed with implant of the pulse generator. At baseline, the SNS group had an average of 9.5 incontinent episodes per week, and the controls had 9.2. Both groups had an average of 3.3 days per week with incontinence. At 12-month follow-up, episodes had decreased to one day per week with 3.1 episodes in the SNS group, but had not changed in the control group (mean, 3.1 days per week with 9.4 episodes). Complete continence was achieved in 22 of the 53 SNS patients (42%) and 13 patients (24%) improved by 75% to 99%. None of the patients had worsening of fecal continence. Adverse events included pain at implant site (6%), seroma (2%), and excessive tingling in the vaginal region (9%).

In 2005, Leroi et al in France published an industry-supported double-blind randomized crossover study. Thirty-four patients had successful temporary percutaneous stimulation and underwent permanent implantation of an SNM device. Following a 1- to 3-month postimplantation period in which the device was turned on, patients had their device turned on for 1 month and off for 1 month, in random order. A total of 24 patients (71%) of randomized patients completed the study. There was a statistically significantly greater decrease in fecal incontinence episodes with the device turned on (p=0.03). However, there was also a large decrease in incontinent episodes for the placebo group. The median frequency of fecal incontinence episodes decreased by 90% when the device was in the on position; it decreased by 76% when the device was in the off position.

Prospective Noncomparative Studies

A key multicenter prospective trial was the 16-site multicenter FDA investigational device exemption study of SNS in 120 patients with fecal incontinence. Findings were initially reported by Wexner et al in 2010. To be included in the study, patients had to complain of chronic fecal incontinence with duration greater than 6 months or for more than 12 months after vaginal childbirth, defined as greater than 2 incontinent episodes on average per week. All patients had failed or were not candidates for more conservative treatments. Exclusion criteria included congenital anorectal malformation; previous rectal surgery, if performed within the last 12 months (or 24 months in case of cancer); defects of the external anal sphincter over 60 degrees; chronic inflammatory bowel disease; visible sequelae of pelvic radiation; active anal abscesses and fistulae; neurologic diseases such as clinically significant peripheral neuropathy or complete spinal-cord injury; and anatomic limitations preventing the successful placement of an electrode. A total of 285 patients were evaluated for potential enrollment; 133 were enrolled and underwent acute test stimulation, and 120 showed at least 50% improvement during the test phase and received a permanent stimulator. Thirty-four of the 120 patients exited the study for a variety of reasons both related (i.e., lack of efficacy in six, implant site infection or skin irritation in five) and unrelated to the implant (i.e., death of a local principal investigator). Analysis based on the initial 133 patients showed a 66% success rate (≥50% improvement), while analysis based on 106 patients who were considered completed cases at 12 months showed an 83% success rate. The success rate based on the 120 patients who received a permanently implanted stimulator would fall between these two figures. Of 106 cases included in the 12-month results, perfect continence (100% improvement) was reported in approximately 40%, while an additional 30% of patients achieved 75% or greater improvement in incontinent episodes. Success was lower in patients with an internal anal sphincter defect (65%, n=20) compared with patients without a defect (87%, n=86).

Three-year and 5-year findings were subsequently published. In 2011, Mellgren et al reported on the 120 patients who received a permanently implanted stimulator. Mean length of follow-up was 3.1 years, and 83 (69%) completed at least part of the three-year follow-up assessment. In an intention-to-treat analysis using the last observation carried forward, 79% of patients experienced at least a 50% reduction in the number of incontinent episodes per week compared with baseline, and 74% experienced at least a 50% reduction in the number of incontinent days per week. In a per-protocol analysis at 3 years, 86% of patients experienced at least a 50% reduction in the number of incontinent episodes per week, and 78% experienced at least a 50% reduction in the number of incontinent days per week. By the 3-year follow-up, a total of 334 adverse events that were potentially device-related had been reported in 99 patients; 67% of these occurred within the first year. The most frequently reported adverse events among the 120 patients were implant site pain (28%); paresthesia (15%), implant site infection (10%), diarrhea (6%), and extremity pain (6%). Six infections required surgical intervention (5 device removals and one device replacement). In 2012, Hull et al reported outcomes in 72 patients (60% of the 120 implanted patients) who had completed a 5-year follow-up visit. Sixty-four (89%) of the patients who contributed bowel diary data at 5 years had at least a 50% improvement from baseline in weekly incontinent episodes, and 26 of the 72 patients (36%) had achieved total continence. It is uncertain whether outcomes differed in the 40% of patients who were missing from the 5-year analysis.

A 2015 study by Altomare et al reported long-term outcome (minimum of 60-month follow-up, median of 84-month follow-up) in patients implanted with a sacral nerve stimulator for fecal incontinence. Patients were identified in a European registry and surveyed. Long-term success was defined as maintaining the temporary stimulation success criteria, i.e., at least 50% improvement in the number of fecal incontinence episodes (or fecal incontinence symptom score) at last follow-up, compared with baseline. A total of 272 patients underwent permanent implantation of SNS device and 228 were available for follow-up. A total of 194 of the 272 (71.3%) implanted patients maintained improvement in the long term.

In 2011, Maeda et al published a systematic review of studies on complications following permanent implantation of a SNS device for fecal incontinence and constipation. The authors identified 94 articles. Most studies addressed fecal incontinence. A combined analysis of data from 31 studies on SNS for fecal incontinence reported a 12% suboptimal response to therapy (149 of 1232 patients). A review of complications reported in the studies found that the most commonly reported complication was pain around the site of implantation, with a pooled rate of 13% (81/621 patients). The most common response to this complication was repositioning the stimulator, followed by explantation of the device and reprogramming. The second most common adverse event was infection, with a pooled rate of 4% (40/1025 patients). Twenty-five of the 40 infections (63%) led to explantation of the device.

Section Summary: Fecal Incontinence

The evidence base consists of 2 RCTs, observational studies including several with long-term follow-up and systematic reviews of RCTs and uncontrolled studies. Taken together, findings of these studies suggest that SNM/SNS improves outcomes when used for the treatment for chronic fecal incontinence in well-selected patients who have failed conservative therapy.

Constipation

Systematic Reviews

In the 2015 Cochrane review by Thaha et al on sacral nerve stimulation for fecal incontinence and constipation in adults, 2 trials on SNM for constipation were included (Dinning et al [2015], along with an additional crossover trial). In one trial, the time with abdominal pain and bloating decreased during the “on” period from 79% to 33%. However, in the larger Dinning et al study, there was no improvement with SNM during the “on” period. The review concluded, “SNS did not improve symptoms in patients with constipation.”

In 2013, Thomas et al published a systematic review of controlled and uncontrolled studies evaluating SNS for treatment of chronic constipation. The authors identified 11 case series and 2 blinded crossover studies. Sample sizes in the case series ranged from 4 to 68 patients implanted with a permanent SNS device; in seven of the eleven studies, fewer than 25 patients underwent SNS implantation. Among the 2 crossover studies, 1 included 2 patients implanted with an SNS device. The other, a 2012 study by Knowles et al, evaluated temporary stimulation in only 14 patients. Patients were included if they were diagnosed with evacuatory dysfunction and rectal hyposensitivity and had failed maximal conservative treatment. They were randomized to 2 weeks of stimulation with the SNS device turned on and 2 weeks with the SNS device turned off, in random order. There was no wash-out period between treatments. The primary efficacy outcome was change in rectal sensitivity and was assessed using 3 measures of rectal sensory thresholds. The study found a statistically significantly greater increase in rectal sensitivity with the device turned on in 2 of the 3 measures. Among the secondary outcome measures, there was a significantly greater benefit of active treatment on the percentage of successful bowel movements per week and the percentage of episodes with a sense of complete evacuation. In addition to its small sample size, the study was limited by the lack of a wash-out period between treatments, i.e., there could have been a carry-over effect when the device was used first in the on position. Moreover, the authors noted that the patients were highly selected; only 14 of the approximately 1800 patients approached met the eligibility criteria and agreed to participate in the study.

Randomized Controlled Trials

In 2017, Zerbib et al reported on a double-blind crossover RCT of SNS in 36 women with refractory constipation. Subjects were eligible if they had chronic constipation (>1 year), with 2 or fewer bowel movements per week, straining to evacuate with more than 25% of attempts, or sensation of incomplete evacuation with more than 25% of attempts, with lack of response to standard therapies. Thirty-six subjects meeting inclusion criteria underwent an initial peripheral nerve evaluation; those who had adequate symptom improvement to a predefined level were offered permanent SNS implant. After a 2 week washout, subjects were randomized to “on” or “off” for 8 weeks, followed by a 2-week washout, when the groups crossed over. Of the 36 patients enrolled, 20 responded and underwent randomization. Four were excluded; 2 due to wound infection, and 1 each to withdrawal of consent and lack of compliance. At 1-year follow-up, a positive response was observed in 12/20 and 11/20 patients after active and sham stimulation periods, respectively (P=0.746).

A larger randomized crossover trial was published by Dinning et al in 2015. The study included patients aged 18 to 75 years with slow transit constipation. Potentially eligible patients completed a 3-week stool diary and, in order to continue participating, they needed to indicate in the diary that they had complete bowel movements less than 3 days per week for at least 2 of the 3 weeks. Patients with metabolic, neurogenic or endocrine disorders known to cause constipation were excluded. Fifty-seven met eligibility criteria and had temporary percutaneous nerve evaluation (PNE), and 55 underwent permanent implantation. In random order, patients received active stimulation (subsensory in Phase 1, suprasensory in Phase 2) or sham stimulation (device was on, but pulse width and frequency was set to 0). The primary outcome measure, determined by stool diaries, was a bowel movement with feelings of complete evacuation more than 2 days per week for at least 2 of 3 weeks; it was only assessed in Phase 2.

Compared with sham stimulation, 16 of 54 patients (29.6%) met the primary outcome during suprasensory stimulation and 11 of 53 patients (20.8%) met it during sham stimulation; the difference was not statistically significant (p=0.23). Other outcomes did not differ significantly with suprastimulation versus sham stimulation and outcomes did not differ in the Phase 1 comparison of subsensory versus sham stimulation.

Case Series

One of the larger case series was published in 2010 by Kamm et al. This was a prospective study conducted at multiple sites in Europe. The study included 62 patients who had idiopathic chronic constipation lasting at least one year and had failed medical and behavioral treatments. Constipation was defined as at least one of the following: fewer than two bowel movements per week, straining to evacuate in at least 25% of attempts or a sensation of incomplete evacuation on at least 25% of occasions. Forty-five of the 62 (73%) met criteria for permanent implantation during the three-week trial period. Criteria included an increase in evacuation frequency to at least three per week, or a 50% reduction in either frequency of straining during evacuation or in episodes with sensation of incomplete evacuation. After a median follow-up of 28 months (range, 1-55 months) after permanent implantation, 39 of 45 (87%) patients were classified as treatment successes (i.e., met same improvement criteria as were used to evaluate temporary stimulation). There was a significant increase in the frequency of bowel movements from a median of 2.3 per week at baseline to 6.6 per week at latest follow-up (p<0.001). The frequency of spontaneous bowel movements (i.e., without use of laxatives or other stimulation) increased from a median of 1.7 per week at baseline to 4.3 per week at last follow-up (p=0.001). A total of 101 adverse events were reported; 40 (40%) of these were attributed to the underlying constipation or an unrelated diagnosis. Eleven serious adverse events related to treatment were reported (the authors did not specify whether any patients experienced more than one serious event). The serious adverse events included a deep postoperative infection (n=2), superficial erosion of lead through the skin (n=1), persistent postoperative pain at the site of implantation (n=2), conditions leading to lead revision (n=4), and device failure (n=2). The study has been criticized for including a large number of patients who had more than two bowel movements per week at study entry.

An additional study, published by Maeda et al in 2010, focused on reporting adverse events. The study was a chart review and included 38 patients with constipation who received permanent SNS after a successful trial period. At the time that charts were reviewed, a mean of 25.7 months had elapsed since implantation. A total of 58 reportable events were identified in 22 of the 38 (58%) patients. A median of two (range, 1 to 9) events per patient were reported; 26 of 58 events (45%) were reported in the first six months after device implantation. The most common reportable events were lack or loss of efficacy (26 of 58 events, 45%), and pain (16 events, 28%). Twenty-eight (48%) of the events were resolved by reprogramming. Surgical interventions were required for 19 (33%) of the events, most commonly permanent electrode replacement (14 events). Three of 38 (8%) patients discontinued use of the device due to reportable events.

<u>Section Summary: Constipation</u>

Four randomized crossover studies are available; 2 had very small sample sizes and the third and fourth did not find a significant difference in outcomes when active SNS was compared with sham stimulation. There are several, mainly small, case series. This represents insufficient evidence to permit scientific conclusions about the effect of SNM/SNS on health outcomes in patients with constipation.

Chronic Pelvic Pain

A 2013 systematic review of studies on nerve stimulation for chronic pelvic pain did not identify any RCTs on SNS for treatment of chronic pelvic pain or bladder pain. The published evidence is limited to case series. For example, in 2012 Martelluci et al reported on 27 patients with chronic pelvic pain (at least 6 months) who underwent testing for SNM implantation. After a 4-week temporary stimulation phase, 16 of 27 patients (59%) underwent implantation of an InterStim device. In the 16 implanted patients, mean pain on a visual analogue scale was 8.1 before implantation and 2.1 at the 6- and 12-month follow-ups. An earlier study by Siegel et al reported on ten patients and stated that 9 of the 10 experienced a decrease in pain with SNS stimulation.

Section Summary: Chronic Pelvic Pain

Data from several small case series with heterogenous patients represents insufficient evidence about the effect of SNM/SNS on health outcomes in patients with chronic pelvic pain. RCTs are needed, especially with sham controls for studies reporting pain as the primary outcome.

Trial Stimulation Techniques

As described in the previous Background section, there are 2 types of trial stimulation before permanent implantation of a neuromodulation device. These are percutaneous nerve evaluation (PNE) and Stage I (lead implantation) of a 2-stage surgical procedure. The PNE was the initial method of trial stimulation and has been the standard of care before permanent implantation of the device. In review articles such as Baxter and Kim 2010, lead migration was described as a potential problem with the PNE technique, but no studies were identified that quantified the rate of lead migration in large numbers of patients. The two-stage surgical procedure is an alternate trial stimulation modality.

Comparative rates of lead migration and rates of progressing to permanent implantation are useful outcomes in that there may be reduced sensitivity of the PNE test due to lead dislodgement. However, due to the potential placebo effect of testing, it is also important to compare the long-term efficacy of SNM after these two trial stimulation techniques. In addition, it would be useful to have data on the optimal approach to using the two-stage surgical procedure. As mentioned previously in the Background section, the two-stage surgical procedure has been used in various ways including instead of PNE, for patients who failed PNE, for patients with an inconclusive PNE, and for patients who had a successful PNE to further refine patient selection.

No RCTs were identified that evaluated long-term health outcomes (e.g., reduction in incontinence symptoms) after trial stimulation with PNE versus Stage I lead implantation. There are limited data on the issue of rates of failure after SNM in patients selected using the 2-stage test. Leong et al, in a single-center prospective study published in 2011, evaluated 100 urge incontinence patients with both PNE and the first stage of the two-stage technique (i.e., patients served as their own controls). Patients were first screened with the PNE and, afterwards, with lead implantation. Response to testing was based on diary data for three consecutive days after receiving each type of lead. In the test phase, 47 patients (47%) had a positive response to PNE, and 69 (69%) had a positive response to the first-stage lead placement test. All patients who responded to PNE also responded to Stage I testing. The 69 patients who responded to Stage I testing underwent implantation. They were then followed for a mean of 26 months, and two patients (3% of those with a positive test) had failed therapy. Although this study showed a low rate of failure, only 22 subjects had a successful test with the Stage I technique but not with PNE. This is a small number of patients on which to base conclusions about the comparative efficacy of the two techniques. In addition, the order of testing could have impacted findings. All patients had PNE testing before first-stage lead implantation and could have been biased by their first test. Stronger study designs would be to randomize the order of testing or to randomize patients to receive 1 type of testing or the other.

In 2002, Scheepens et al conducted an analysis of 15 patients with urinary incontinence or retention that had a good initial response to PNE but then failed PNE in the longer term (i.e., days 4 to 7 of testing). These 15 patients underwent Stage I of the 2-stage technique. One patient failed the first stage and was explanted. Of the remaining 14 patients, 2 were explanted later due to lack of efficacy of SNM. The other 12 patients were followed for a mean of 4.9 years and voiding diary data showed improvement in nearly all incontinence symptoms. There was a low failure rate after Stage I testing, but this is a small sample size, and Stage I testing was not compared with another trial stimulation method (e.g., PNE).

In 2010, Marcelissen et al published findings in 92 patients with urinary symptoms who underwent trial evaluation for SNM treatment. Patients initially underwent PNE (n=76) or Stage I surgery (n=16). Patients who had a negative PNE (n=41) then underwent Stage I evaluation. A total of 11 of 16 (63%) patients had a positive initial Stage I test and were implanted with a SNM device. Thirty-five of 76 (46%) patients had a positive initial PNE test and underwent permanent implantation. There were 41 patients (54% of those undergoing PNE) who had a negative test and then had Stage I surgical evaluation. Eighteen of 41 (44%) had a positive Stage I test and underwent implantation. Altogether there were 64 patients who underwent implantation of an SNM device. Mean follow-up was 51 months. Thirty-eight of 64 patients (59%) implanted experienced clinical success at last follow-up, defined as greater than 50% improvement in symptoms reported in a voiding diary. Clinical success rate was not reported separately by trial stimulation method.

Several studies, e.g., Borawski et al (2007) and Bannowsky et al (2008), compared the response rates during the test phase in patients with urinary incontinence symptoms and found higher rates of response with the Stage I test than with PNE. In these studies, more people who received the Stage I test went on to undergo implantation. The Borawski et al study was an RCT with 30 patients (13 received PNE and 17 received the Stage I test). The Bannowsky et al study was not randomized; 42 patients received a PNE, and 11 patients received a Stage I test. Neither study, however, followed patients once they had a device implanted, so they do not provide data on the relative success rate of SNM after these 2 test procedures. With this type of study (i.e., without follow-up after implantation), it is not possible to conclude whether the 2-stage procedure reduced false negatives (i.e., selected more people who might benefit) or increased false negatives (i.e., selected more people who might go on to fail).

No published studies were identified that compare different trial stimulation techniques in patients with non-urinary conditions (e.g., fecal incontinence).

Summary of Evidence

For individuals with urinary incontinence who have failed conservative treatment who receive sacral nerve neuromodulation (SNM), the evidence includes randomized controlled trials and systematic reviews. Relevant outcomes are symptoms, morbid events, and treatment-related morbidity. Results from the RCTs and case series with long-term follow-up suggest that SNM reduces symptoms of urge incontinence, urgency-frequency syndrome, nonobstructive urinary retention, and overactive bladder in selected patients. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with fecal incontinence who have failed conservative treatment who receive SNM, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, morbid events, and treatment-related morbidity. Although relatively small, the available trials are at low risk of bias and demonstrate improvements in incontinence relative to alternatives. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with constipation who receive SNM, the evidence includes RCTs and systematic reviews. Relevant outcomes are symptoms, morbid events, and treatment-related morbidity. The available trials have not consistently reported improvements in outcomes with SNM. Additional studies are needed to demonstrate outcome improvements for this technology. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with chronic pelvic pain who receive SNM, the evidence is limited to case series. Relevant outcomes are symptoms, morbid events, and treatment-related morbidity. The evidence is insufficient to determine the effects of the technology on health outcomes.

Practice Guidelines and Position Statements

American Urological Association

In 2014, the American Urological Association issued an updated guideline on diagnosis and treatment of overactive bladder. The guideline states that sacral neuromodulation may be offered as a third-line treatment in carefully selected patients with severe refractory symptoms or in those who are not candidates for second-line therapy (e.g., oral anti-muscarinics, oral β_3-adrenoceptor agonists or transdermal oxybutynin) and are willing to undergo surgery.

National Institute for Health and Care Evidence

The National Institute for Health and Care Excellence issued guidance on management of fecal incontinence in 2007. It recommended:

> “a trial of temporary sacral nerve stimulation should be considered for people with faecal incontinence in which sphincter surgery is deemed inappropriate…. All individuals should be informed of the potential benefits and limitations of this procedure and should undergo a trial stimulation period of at least 2 weeks to determine if they are

likely to benefit. People with faecal incontinence should be offered sacral nerve stimulation on the basis of their response to percutaneous nerve evaluation during specialist assessment, which is predictive of therapy success."

American College of Gastroenterology (ACG)
A 2004 practice guideline on the diagnosis and management of fecal incontinence found limited evidence in favor of SNS. The ACG concluded that the precise indication for SNS, its comorbidity, its long-term outcome, and efficacy remain to be defined.

American College of Obstetricians and Gynecologists (ACOG)
- A 2005 position statement considered sacral nerve neuromodulation to be beneficial for treating chronic voiding dysfunction.
- A 2004 position statement recommended that SNS be considered as a treatment option for chronic pelvic pain. According to the ACOG website, accessed in March 2014, the practice bulletin on chronic pelvic pain is no longer maintained.

Pelvic Floor Society
The Pelvic Floor Society conducted a systematic review as the basis for practice recommendations on the use of SNS for the treatment of constipation. They systematic review assessed 7 observational studies, all generally of poor quality due to inadequate description of methods. Due to inconsistent reporting on harms and treatment success, and heterogeneity in the patient populations, the Society could not recommend SNS.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Key Words:
Interstim, incontinence, sacral nerve stimulation, sacral neuromodulation, InterStim® II, InterStim iCon™ Patient Programmer, fecal incontinence, urinary incontinence

Approved by Governing Bodies:
In 1997, the Medtronic InterStim® Sacral Nerve Stimulation system received U.S. Food and Drug Administration (FDA) approval for marketing for the indication of urinary urge incontinence in patients who have failed or could not tolerate more conservative treatments. In 1999, the device received FDA approval for the additional indications of urgency-frequency and urinary retention in patients without mechanical obstruction. There has also been research interest in using the device as a treatment of fecal incontinence, constipation, and chronic pelvic pain. In 2006, the Medtronic Interstim® II System received FDA approval for treatment of intractable cases of overactive bladder and urinary retention. The new device is smaller and lighter than the original system and is reported to be suited for those with lower energy requirements or small stature. The device also includes updated software and programming options. All other uses of this device (e.g., fecal incontinence or constipation) would be off-label. In 2011, the FDA approved the use of InterStim® for the treatment of chronic fecal

incontinence in patients who have failed or are not candidates for more conservative treatments. The InterStim® device has not been specifically approved by FDA for treatment of chronic pelvic pain.

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.
ITS: Home Policy provisions apply
FEP contracts: Special benefit consideration may apply. Refer to member's benefit plan.

Current Coding:

CPT codes:

64561	Percutaneous implantation of neurostimulator electrode array; sacral nerve (transforaminal placement) including image guidance, if performed
64581	Incision for implantation of neurostimulator electrode~~s~~ array; sacral nerve
64585	Revision or removal of peripheral neurostimulator electrode~~s~~ 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
95970	Electronic analysis of implanted neurostimulator pulse generator system (e.g. rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple or complex brain, spinal cord, or peripheral (i.e. cranial nerve, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without programming, first hour
95971	Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); simple spinal cord, or peripheral (i.e., peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming
95972	Electronic analysis of implanted neurostimulator pulse generator system (e.g. rate, pulse amplitude, pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); complex, spinal cord, or peripheral (i.e. peripheral

nerve, sacral nerve, neuromuscular) (except cranial nerve) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming, ~~up to one hour~~

HCPCS:

A4290	Sacral nerve stimulation test lead, each
E0745	Neuromuscular stimulator, electrical shock unit
E1399	Durable medical equipment, miscellaneous
L8680	Implantable neurostimulator electrode, each
L8681	Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
L8683	Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver
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
L8689	External recharging system for battery (internal) for use with implantable neurostimulator, replacement only
L8695	External recharging system for battery (external) for use with implantable neurostimulator, replacement only

Previous Coding:

CPT Codes:

95973	; each additional 30 minutes after first hour (list separately in addition to code for primary procedure **(Deleted effective 01/01/2016)**

References:

1. Aboseif S, Tamaddon K, et al. Sacral neuromodulation in functional urinary retention: An effective way to restore voiding, BJU International, November 2002; 90(7): 662-5. (Abstract)
2. Altomare DF, Giuratrabocchetta S, Knowles CH, et al. Long-term outcomes of sacral nerve stimulation for faecal incontinence. Br J Surg. Mar 2015; 102(4):407-415.
3. American College of Obstetricians and Gynecologists. Urinary incontinence in women. Obstet Gynecol 2005; 105(6):1533-45.
4. American College of Obstetricians and Gynecologists (ACOG). Practice Bulletin List of Titles- March 2014. Available online at: www.acog.org/~/media/List%20of%20Titles/PBListOfTitles.pdf?dmc=1&ts=20140311T1415320475.

5. American Urological Association (AUA). Guideline on Diagnosis and Treatment of Overactive Bladder. 2014; //www.auanet.org/education/guidelines/overactive-bladder.cfm.
6. Amundsen CL, Richter HE, Menefee SA, et al. OnabotulinumtoxinA vs Sacral Neuromodulation on Refractory Urgency Urinary Incontinence in Women: A Randomized Clinical Trial. JAMA. Oct 04 2016; 316(13):1366-1374.
7. Aslan AR and Kogan BA. Conservative management in neurogenic bladder dysfunction, Current Opinion in Urology, November 2002; 12(6): 473-7.
8. Bannowsky A, Wefer B, Braun PM et al. Urodynamic changes and response rates in patients treated with permanent electrodes compared to conventional wire electrodes in the peripheral nerve evaluation test. World J Urol. 2008; 26(6):623-6.
9. Baxter C, Kim JH. Contrasting the percutaneous nerve evaluation versus staged implantation in sacral neuromodulation. Curr Urol 2010; 11(5):310-4.
10. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Sacral nerve stimulation for the treatment of urge incontinence. TEC Assessments 1998; Volume 13:Tab 18.
11. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Sacral nerve stimulation for the treatment of refractory urinary urgency/frequency in adults. TEC Assessments. 2000; Volume 15: Tab 7.
12. Borawski KM, Foster RT, Webster GD et al. Predicting implantation with a neuromodulator using two different test stimulation techniques: a prospective randomized study in urge incontinent women. Neurourol Urodyn 2007; 26(1):14-8.
13. Brazzelli M, Murray A, Fraser C. Efficacy and safety of sacral nerve stimulation for urinary urge incontinence: a systematic review. J Urol 2006; 175(3 pt 1):835-41.
14. Comiter CV, Sacral neuromodulation for the symptomatic treatment of refractory interstitial cystitis: a prospective study. J Urol 2003; 169(4):1369-73.
15. Dinning PG, Hunt L, Patton V, et al. Treatment efficacy of sacral nerve stimulation in slow transit constipation: a two-phase, double-blind randomized controlled crossover study. Am J Gastroenterol. May 2015; 110(5):733-740.
16. Food and Drug Administration (FDA). Summary of Safety and Effectiveness: Medtronic Interstim System for Urinary Control. //www.accessdata.fda.gov/cdrh_docs/pdf/P970004S004b.pdf. Accessed April 29, 2015.
17. Ganio E, Luc AR, Clerioco G, Trompetto M. Sacral nerve stimulation for treatment of fecal incontinence, Dis Colon Rectum 2001; 44: 619-31.
18. Ganio E, Ratto C, Masin A, et al. Neuromodulation for fecal incontinence: Outcome in 16 patients with definitive implant, Dis Colon Rectum 2001; 44: 619-31.
19. George AT, Kalmar K, Panarese A et al. Long-term outcomes of sacral nerve stimulation for fecal incontinence. Dis Colon Rectum 2012; 55(3):302-6.
20. Groen J, Blok BF, Bosch JL. Sacral neuromodulation as treatment for refractory idiopathic urge urinary incontinence: 5-year results of a longitudinal study in 60 women. J Urol. 2011; 186(3):954-9.
21. Hassouna MM, Siegel SW, Nyeholt AA, et al. Sacral neuromodulation in the treatment of urgency-frequency symptoms: A multicenter study on efficacy and safety, J Urol 2000; 163: 1849-54.
22. Herbison GP and Arnold EP. Sacral neuromodulation with implanted devices for urinary storage and voiding dysfunction in adults. Cochrane Database Syst Rev, April 2009; (2): CD004202.

23. Hull T, Giese C, Wexner SD et al. Long-term durability of sacral nerve stimulation therapy for chronic fecal incontinence. Dis Colon Rectum 2013; 56(2):234-45.
24. Janknegt RA, Hassouna MM, Siegel SW, et al. Long-term effectiveness of sacral nerve stimulation for refractory urge incontinence, Eur Urol 2001, 39: 101-106.
25. Jonas U. Efficacy of sacral nerve stimulation for urinary retention: Results 18 months after implantation, Journal of Urology, January 2001; 165(1): 15-9. (Abstract)
26. Kamm MA, Dudding TC, Melenhorst J, et al. Sacral nerve stimulation for intractable constipation. Gut. Mar 2010;59(3):333-340.
27. Kenefick NJ, Nicholls RJ, Cohen RG, Kamm MA. Permanent sacral nerve stimulation for treatment of idiopathic constipation, Br J Surg 2002; 89: 882-88.
28. Kenfick NJ, Nicholls RJ, Cohen RG et al. Medium term results of permanent sacral nerve stimulation for faecal incontinence. Br J Surg 2002; 89(7):896-901.
29. Knowles CH, Thin N, Gill K et al. Prospective randomized double-blind study of temporary sacral nerve stimulation in patients with rectal evacuatory dysfunction and rectal hyposensitivity. Ann Surg 2012; 255(4):643-9.
30. Leong RK, De Wachter SG, Nieman FH et al. PNE versus 1st stage tined lead procedure: a direct comparison to select the most sensitive test method to identify patients suitable for sacral neuromodulation therapy. Neurourol Urodyn 2011; 30(7):1249-52.
31. Leroi AM, Damon H, Faucheron JL et al. Sacral nerve stimulation in faecal incontinence: position statement based on a collective experience. Colorectal Dis 2009; 11(6):572-83.
32. Leroi AM, Parc Y, Lehur PA et al. Efficacy of sacral nerve stimulation for fecal incontinence: results of a multicenter double-blind crossover study. Ann Surg 2005; 242(5):662-9.
33. Maeda Y, Matzel K, Lundby L et al. Postoperative issues of sacral nerve stimulation for fecal incontinence and constipation: a systematic literature review and treatment guideline. Dis Colon Rectum 2011; 54(11):1443-60.
34. Maeda Y, Lundby L, Buntzen S, et al. Sacral nerve stimulation for constipation: suboptimal outcome and adverse events. Dis Colon Rectum. Jul 2010; 53(7):995-999.
35. Maher CF, Carey MP, Dwyer PL et al. Percutaneous sacral nerve root neuromodulation for intractable interstitial cystitis. J Urol 2001; 165(3):884-6.
36. Malouf AJ, Wiesel PH, Nicholls T, et al. Short-term effects of sacral nerve stimulation for idiopathic slow transit constipation, Word J Surg 2002; 26: 166-70.
37. Marcelissen TA, Leong RK, de Bie RA et al. Long-term results of sacral neuromodulation with the tined lead procedure. J Urol 2010; 184(5):1997-2000.
38. Martellucci J, Naldini G, Carriero A. Sacral nerve modulation in the treatment of chronic pelvic pain. Int J Colorectal Dis 2012; 27(7):921-6.
39. Matzel KE, Kamm MA, Strosser M et al. Sacral spinal nerve stimulation for fecal incontinence: multicentre study. Lncet 2004; 363(9417):1270-6.
40. Matzel KE, Lux P, Heuer S, et al. Sacral nerve stimulation for faecal incontinence: Long-term outcome. Colorectal Dis, July 2009; 11(6): 636-641.
41. Medtronic. Interstim Therapy: Sacral nerve stimulation (SNS) for urinary control, 2001 Compendium of Key Abstracts, www.interstim.com.
42. Medtronic. Summary of multi-center clinical study, Medtronic Neurological, Minneapolis, MD, www.interstim.com.
43. Mellgren A, Wexner SD, Coller JA et al. Long-term efficacy and safety of sacral nerve stimulation for fecal incontinence. Dis Colon Rectum 2011; 54(9):1065-75.

44. Michelsen HB, Thompson-Fawcett M, Lundby L et al. Six years of experience with sacral nerve stimulation for fecal incontinence. Dis Colon Rectum 2010; 53(4):414-21.
45. Mowatt G, Glazener C, Jarrett M. Sacral nerve stimulation for fecal incontinence and constipation in adults: a short version Cochrane review. Neurolurol Urodyn 2008; 27(3):155-61.
46. National Institute for Clinical Evidence (NICE). Sacral nerve stimulation for faecal incontinence. Interventional Procedure Guidance 99; 2004. Available at: www.nice.org.uk/nicemedia/live;11079/30919/30919.pdf.
47. Noblett K, Siegel S, Mangel J, et al. Results of a prospective, multicenter study evaluating quality of life, safety, and efficacy of sacral neuromodulation at twelve months in subjects with symptoms of overactive bladder. Neurourol Urodyn. Dec 24 2014.
48. Payne CK, Whitmore KE, Diokno AC et al. Sacral neuromodulation in patients with interstitial syctitis: a multicenter clinical trial. Neurool Urodyn 2001; 20:554-5.
49. Pilkington SA, Emmett C, Knowles CH et al. Surgery for constipation; systematic reviews and practice recommendations: Results V: Sacral Nerve Stimulation. Colorectal Dis. Sep 2017; 19 (Suppl 3): 92-100.
50. Rao SS; American College of Gastroenterology Practice Parameters Committee. Diagnosis and management of fecal incontinence. American College of Gastroenterology Practice Parameters Committee. Am J Gastroenterol 2004; 88(8); 1585-604. Available at: www.gi.org/physicians/guidelines/FecalIncontinence.pdf.
51. Rosen HR, Urbarz C, Holzer B, et al. Sacral nerve stimulation as a treatment for fecal incontinence, Gastroenterol 2001; 121: 536-41.
52. Siegel S, Noblett K, Mangel J et al. Results of a prospective, randomized, multicenter study evaluating sacral neuromodulation with InterStim therapy compared with standard medical therapy at 6-months in subjects with mild symptoms of overactive bladder. Neurourol Urodyn 2014.
53. Scheepens WA, Van Koeveringe GA, De Bie RA et al. Long-term efficacy and safety results of the two-stage implantation technique in sacral neuromodulation. BJU Int 2002; 90(9):840-5.
54. Schmidt RA, Jonas U, Oleson KA, et al. Sacral nerve stimulation for treatment of refractory urinary urge incontinence, J Urol 1999; 162: 352-7.
55. Siegel S, Paszkiewicz E, Kirkpatrick C, et al. Sacral nerve stimulation in patient with chronic intractable pelvic pain, J Urol 2001; 166: 1742-54.
56. Sutherland SE, Lavers A, Carlson A, et al. Sacral nerve stimulation for voiding dysfunction: One institution's 11-year experience. Neurourol Urodyn 2007; 26(1): 19-28.
57. Tan E, Ngo NT, Darzi A et al. Meta-analysis: sacral nerve stimulation versus conservative therapy in the treatment of faecal incontinence. Int J Colorectal Dis 2011; 26(3):275-94.
58. Tirlapur SA, Vlismas A, Ball E et al. Nerve stimulation for chronic pelvic pain and bladder pain syndrome: a systematic review. Acta Obstet Gynecol Scand 2013; 92(8):881-7.
59. Thaha MA, Abukar AA, Thin NN, et al. Sacral nerve stimulation for faecal incontinence and constipation in adults. Cochrane Database Syst Rev. Aug 24 2015; (8):CD004464.
60. Thomas GP, Dudding TC, Rahbour G et al. Sacral nerve stimulation for constipation. Br J Surg 2013; 100(2):174-81.
61. Thin NN, Horrocks EJ, Hotouras A et al. Systematic review of the clinical effectiveness of neuromodulation in the treatment of faecal incontinence. Br J Surg 2013; 100(11):1430-47.

62. Tjandra JJ, Chan MK, Yeh CH and Murray-Green C. Sacral nerve stimulation is more effective than optimal medical therapy for severe fecal incontinence: A randomized, controlled study. Dis Colon Rectum, May 2008; 51(5): 494-502.
63. Wallace PA, Lane FL and Noblett KL. Sacral nerve neuromodulation in patients with underlying neurologic disease. Am J Obstet Gynecol, July 2007; 197(1): 96.
64. Weil EG, Ruiz-Cerda JL, Eerdmans PH, et al. Sacral root neuromodulation in the treatment of refractory urinary urge incontinence: A prospective randomized clinical trial, Eur Urol 2000; 37(2): 161-71.
65. Wexner SD, coller JA, Devroede G et al. Sacral nerve stimulation for fecal incontinence: results of a 120-patient prospective multicenter study. Ann Surg 2010; 25(3):441-9.
66. White WM, Mobley JD III, Doggweiler R, et al. Incidence and predictors of complications with sacral neuromodulation. Urology, April 2009; 73(4): 731-735.
67. Zerbib F, Siproudhis L, Lehur PA, et al. Randomized clinical trial of sacral nerve stimulation for refractory constipation. Br J Surg. Oct 25 2016.

Policy History:

Medical Policy Group, October 2003
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Medical Policy Group, June 2012 **(3):** 2012 Updates-Description, Policy, Key Points, & References
Medical Policy Group, December 2012 **(3)**: 2013 Coding Update: Verbiage change to 64561
Medical Policy Panel, April 2013
Medical Policy Group, April 2013 **(3)**: 2013 Updates to Key points and References; minor clarification to policy statement
Medical Policy Group, May 2014 **(5):** 2014 Coding Update: Deleted code L8680 effective July 1, 2014.

Medical Policy Group, June 2014 **(5):** 2014 Quarterly Coding Update: Code L8680 did not delete; removed delete date.
Medical Policy Panel, April 2014
Medical Policy Group, July 2014 **(4)**: Added indication of overactive bladder to policy statement. Updated Approved Governing Bodies, Key Points and References.
Medical Policy Administration Committee, August 2014
Available for comment July 28 through September 8, 2014
Medical Policy Group, November 2014: 2015 Coding Update – Code 95972-removed 'simple' and 'brain' and all references to cranial. Changed from 'first hour' to 'up to one hour'.
Medical Policy Group, March 2015 **(6):** Rearranged policy statement; no change to policy intent.
Medical Policy Panel, July 2015
Medical Policy Group, July 2015 **(6):** Added/clarified statement on fecal incontinence policy statement and changed trial stimulation period to 48 hours on both urinary and fecal policy statements; updates to Key Points, Coding and References.
Medical Policy Administration Committee, July 2015
Available for comment July 21 through September 3, 2015
Medical Policy Group, November 2015: 2016 Annual Coding Update. Created a previous coding section and moved cpt code 95973 from current coding to previous coding section. Revised CPT code 95972.
Medical Policy Panel, January 2017
Medical Policy Group, January 2017 (**6**): Updates to Key Points, Practice Guidelines and References. No change to policy statement.
Medical Policy Panel, April 2018
Medical Policy Group, April 2018 **(6)**: Updates to Description, Key Points, Practice Guidelines, Key Words and References; Removed old policy statement from 2013.
