BlueCross BlueShield of Louisiana

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Sacral Nerve Neuromodulation/Stimulation

Policy # 00108
Original Effective Date: 03/25/2002
Current Effective Date: 06/18/2014

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc.(collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage
Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Urinary Incontinence and Non-obstructive Retention
Based on review of available data, the Company may consider a trial period of sacral nerve neuromodulation (SNM) with either percutaneous nerve stimulation or a temporarily implanted lead in patients who meet all of the following criteria to be **eligible for coverage**:

- There is a diagnosis of at least one of the following;
  - Urge incontinence
  - Urgency-frequency syndrome
  - Non-obstructive urinary retention; and
- There is documented failure or intolerance to at least two 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); and
- The patient is an appropriate surgical candidate; and
- Incontinence is not related to a neurologic condition.

Based on review of available data, the Company may consider permanent implantation of a sacral nerve neuromodulation (SNM) device in patients who meet all of the following criteria to be **eligible for coverage**:

- All of the criteria above are met; and
- A trial stimulation period demonstrates at least 50% improvement in symptoms over a period of at least 1 week.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers other urinary/voiding applications of sacral nerve neuromodulation (SNM), 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 to be **investigational.***

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Fecal Incontinence
Based on review of available data, the Company may consider a trial period of sacral nerve neuromodulation (SNM) with either percutaneous nerve stimulation or a temporarily implanted lead in patients who meet all of the following criteria to be **eligible for coverage**:

- There is a diagnosis of chronic fecal incontinence of greater than 2 incontinent episodes on average per week with duration greater than 6 months or for more than 12 months after vaginal childbirth; and
- 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, performed more than 12 months [or 24 months in case of cancer] previously); and
- The patient is an appropriate surgical candidate; and
- 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; and
- Incontinence is not related to a neurologic condition.

Based on review of available data, the Company may consider permanent implantation of a sacral nerve neuromodulation (SNM) device in patients who meet all of the following criteria to be **eligible for coverage**:

- All of the criteria above are met; and
- A trial stimulation period demonstrates at least 50% improvement in symptoms over a period of at least 1 week.

When Services Are Considered Investigational
Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers sacral nerve neuromodulation (SNM) in the treatment of chronic constipation or chronic pelvic pain to be **investigational.***

Background/Overview

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

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

The SNM 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 4-7 days. This lead is connected to an external stimulator, which is carried by patients in their pocket or on their belt. 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 symptom 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.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
In 1997, the Medtronic InterStim®‡ Sacral Nerve Stimulation system received U.S. 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. 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. In 2011, the Medtronic InterStim System received FDA approval for the indication of chronic fecal incontinence in patients who have failed or could not tolerate more conservative treatments.

Note: This policy does not address pelvic floor stimulation which refers to electrical stimulation of the pudendal nerve. In addition, this policy does not address devices that provide direct sacral nerve stimulation in patients with spinal cord injuries. An example of such a device is the VOCARE®‡ sacral nerve stimulator, which is intended for patients with complete spinal cord injury and neurogenic bladder.

Centers for Medicare and Medicaid Services (CMS)
Effective January 1, 2002, SNS is covered for the treatment of urinary urge incontinence, urgency-frequency syndrome, and urinary retention. SNS involves both a temporary test stimulation to determine if an implantable stimulator would be effective and a permanent implantation in appropriate candidates. Both the test and the permanent implantation are covered.

The following limitations for coverage apply to all three indications:

- Patients must be refractory to conventional therapy (documented behavioral, pharmacologic and/or surgical corrective therapy) and be appropriate surgical candidates such that implantation with anesthesia can occur.
- Patients with stress incontinence, urinary obstruction, and specific neurologic diseases (e.g., diabetes with peripheral nerve involvement) that are associated with secondary manifestations of the above three indications are excluded.
- Patients must have had successful test stimulation in order to support subsequent implantation. Before patients are eligible for permanent implantation, they must demonstrate a 50% or greater improvement through test stimulation.
- Improvement is measured through voiding diaries. Patients must be able to demonstrate adequate ability to record voiding diary data such that clinical results of the implant procedure can be properly evaluated.

Rationale/Source

The most recent literature search was for the period February 2012 through March 13, 2013.

Urinary Incontinence
Two randomized controlled trials (RCTs) on sacral nerve neuromodulation for urinary incontinence have been conducted. The larger study was sponsored by Medtronic and submitted to the U.S. FDA 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 to 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 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 the 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 to a control group, patients with implants reported significant improvements in quality of life, as evaluated by the Short Form-36 (SF-36) 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, as compared to those receiving conservative therapy. The magnitude of effect was substantial. This study provides further evidence of the beneficial effect of SNM for urinary urge incontinence.

Case series continue to be published. A 2011 series by Groen and colleagues 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 1 month and gradually decreased to 37 (62%) at 5 years. The number of women who were completely continent was 15 (25%) at 1 month and 9 (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 and colleagues. 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 7–84), 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.

A 2009 Cochrane review evaluated the literature on implanted devices for urinary storage and voiding dysfunction in adults. The authors stated that, in spite of methodologic problems (generally poor quality studies), the evidence “seems clear that continuous stimulation offers benefits for carefully selected people with overactive bladder syndrome and for those with urinary retention but no structural obstruction.” They

concluded that while some people benefit, more research is needed to improve patient selection, to carry out the implant, and to find why so many fail.

In summary, data from RCTs and case series with long-term follow-up suggest that sacral nerve neuromodulation reduces symptoms of urge incontinence, urgency-frequency syndrome, and non-obstructive urinary retention in selected patients.

Fecal Incontinence
In 2011, Tan and colleagues published a meta-analysis of randomized trials and observational studies published between 2000 and 2008 on sacral nerve neuromodulation 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. 2008), discussed in more detail below. In the 34 studies, a total of 944 patients underwent temporary 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 2 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 to 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 to conservative therapy (weighted mean difference: -10.57, 95% CI: -11.89 to -9.24, $p<0.001$).

In 2008, Tjandra and colleagues published an RCT with 120 patients with severe fecal incontinence. Patients were randomly assigned to receive sacral nerve stimulation 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 1 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%).

A key observational study was the 16-site multicenter FDA investigational device exemption study of SNS in 120 patients with fecal incontinence. Findings were initially reported by Wexner and colleagues 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 6 and implant site infection or skin irritation in 5) 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 2 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 five-year findings were subsequently published. In 2011, Mellgren and colleagues 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 3-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 to 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 1 device replacement). In 2012, Hull and colleagues 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.

Several small case series have reported long-term follow-up. For example, in 2012, George and colleagues reported on 23 patients who underwent SNS for fecal incontinence after a successful trial of temporary stimulation. Over a median follow-up of 9.5 years, 12 of the 23 patients (48%) maintained full continence. Two patients lost efficacy at 4 years and 5 years, respectively and had the device removed. Nine patients required a change of battery after a mean of 7 years. Three patients died of unrelated causes. In 2008, Matzel and colleagues reported long-term outcomes from 12 patients with severe incontinence (average of 54% incontinent episodes per week) who underwent SNS between 1994 and 1999. In 3 patients, the device was removed because of pain or neurologic disease; the remaining 9 patients showed continued efficacy over an average 10-year follow-up (range 7–14 years). Complete continence was achieved in 5 patients

(42% of 12), and 3 patients (25%) had less than 10% incontinent episodes. Pulse generator exchange was required in 8 of the 9 patients after a mean of 7 years for battery fatigue.

In 2011, Maeda and colleagues 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. The vast majority of 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 1,232 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 of13% (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.

In summary, the evidence base consists of longer term results from one RCT with 120 patients, prospective case series, and a pooled analysis of data from the RCT and observational studies. Taken together, findings of these studies suggest that sacral nerve neuromodulation/stimulation improves outcomes when used for the treatment for chronic fecal incontinence in well-selected patients who have failed conservative therapy.

Constipation
In 2013, Thomas and colleagues published a systematic review of controlled and uncontrolled studies evaluating sacral nerve stimulation 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 7 of the 11 studies, fewer than 25 patients underwent SNS implantation. Among the 2 crossover studies, one included 2 patients implanted with an SNS device. The other, a 2012 study by Knowles and colleagues, 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 1,800 patients approached met the eligibility criteria and agreed to participate in the study.

One of the larger case series was published in 2010 by Kamm and colleagues. This was a prospective study conducted at multiple sites in Europe. The study included 62 patients who had idiopathic chronic constipation lasting at least 1 year and had failed medical and behavioral treatments. Constipation was defined as at least one of the following: fewer than 2 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 3-week trial period. Criteria included an increase in evacuation frequency to at least 3 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; $p=0.0004$. 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 1 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 2 bowel movements per week at study entry.

An additional study, published by Maeda and colleagues 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 2 (range 1-9) events per patient were reported; 26 of 58 events (45%) were reported in the first 6 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.

In summary, only 2 small controlled studies are available, both crossover studies; 1 had only 2 patients and the other had methodologic limitations. In addition, there are several, mainly small, case series. This represents insufficient evidence to permit scientific conclusions about the effect of sacral nerve neuromodulation/stimulation on health outcomes in patients with constipation.

Chronic Pelvic Pain

Several case series have evaluated sacral neuromodulation for treating chronic pelvic pain. For example, in 2012 Martelluci and colleagues 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 (VAS) was 8.1 prior to implantation and 2.1 at the 6- and 12-month follow-ups. An earlier study by Siegel and colleagues reported on 10 patients and stated that 9 of the 10 experienced a decrease in pain with SNS stimulation.

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In summary, data from several small case series with heterogenous patients represents insufficient evidence about the effect of sacral nerve neuromodulation/stimulation on health outcomes in patients with chronic pelvic pain.

Trial Stimulation Techniques

As described in the Background section above, there are 2 types of trial stimulation before permanent implantation of a neuromodulation device. These are PNE and stage 1 (lead implantation) of a 2-stage surgical procedure. The PNE was the initial method of trial stimulation and has been the standard of care prior to permanent implantation of the device. There are concerns about possible suboptimal sensitivity of the PNE test due to lead migration, and the stage-1 lead implantation 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 2 trial stimulation techniques. In addition, it would be useful to have data on the optimal approach to using the 2-stage surgical procedure. As mentioned previously in the background section, the 2-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-1 lead implantation. There are limited data on the issue of rates of failure after SNM in patients selected using the 2-stage test. Leong and colleagues, in a single-center prospective study published in 2011, evaluated 100 urge incontinence patients with both PNE and the first stage of the 2-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 3 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-1 testing. The 69 patients who responded to stage-1 testing underwent implantation. They were then followed for a mean of 26 months, and 2 patients (3% of those with a positive test) had failed therapy. Although this study showed a low rate of failure, only 22 individuals had a successful test with the stage-1 technique but not with PNE. This is a small number of patients on which to base conclusions about the comparative efficacy of the 2 techniques. In addition, the order of testing could have impacted findings. All patients had PNE testing prior to 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 one type of testing or the other.

In 2002, Scheepens and colleagues conducted an analysis of 15 patients with urinary incontinence or retention who had a good initial response to PNE but then failed PNE in the longer term (i.e., days 4-7 of testing). These 15 patients underwent stage 1 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 sacral neuromodulation. 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-1 testing, but this is a small sample size, and stage-1 testing was not compared to another trial stimulation method, e.g., PNE.

In 2010, Marcelissen and colleagues published findings in 92 patients with urinary symptoms who underwent trial evaluation for SNM treatment. Patients initially underwent PNE (n=76) or stage-1 surgery (n=16). Patients who had a negative PNE (n=41) then underwent stage-1 evaluation. A total of 11 of 16 (63%) patients had a positive initial stage-1 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-1 surgical evaluation. Eighteen of 41 (44%) had a positive stage-1 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 and colleagues (2006) and Bannowsky and colleagues (2008), compared the response rates during the test phase in patients with urinary incontinence symptoms and found higher rates of response with the stage-1 test than with PNE. In these studies, more people who received the stage-1 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-1 test). The Bannowsky et al. study was not randomized; 42 patients received a PNE, and 11 patients received a stage-1 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).

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. No published studies were available comparing trial stimulation techniques in patients with non-urinary conditions e.g., fecal incontinence.

Clinical Input Received through Physician Medical Societies and Academic Medical Centers
In response to requests, input was received through 4 Physician Specialty Societies and 2 Academic Medical Centers while this policy was under review in 2012. While the various Physician Specialty Societies and Academic Medical Centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the Physician Specialty Societies or Academic Medical Centers, unless otherwise noted. Reviewers from 2 Specialty Societies and 2 Academic Medical Centers provided opinions regarding the possible medical necessity of implantable leads for test stimulation, as part of a 2-stage process for device implantation. All 4 respondents supported the use of implantable leads for test stimulation as an alternative to percutaneous test stimulation, for patients who failed percutaneous test stimulation and/or for patients with inconclusive percutaneous test stimulation. Reasons for support included a longer period of

interrupted treatment with stage-1 stimulation due to less lead migration and a higher rate of positive tests compared to percutaneous test stimulation.

Summary

There is sufficient evidence to conclude that sacral nerve neuromodulation/stimulation is effective and safe in selected patients with urge incontinence, urgency-frequency, and non-obstructive urinary retention. In addition, the evidence is considered sufficient for sacral nerve neuromodulation to be an option for the treatment for chronic fecal incontinence in well-selected patients who have failed conservative therapy. Therefore, SNM may be considered medically necessary under specific conditions in the above patients. Not all patients will benefit, and the adverse event rate for this procedure is high. Patients should therefore be provided with adequate information to make an informed choice regarding the potential risks and benefits of this procedure.

Limited evidence reports that more patients have a positive stimulation trial when stage-1 surgery is used compared to PNE and that the majority of patients with a positive stage-1 test experience a reduction in symptoms after permanent implantation. This evidence does not determine with certainty that health outcomes are improved with the stage-1 trial stimulation. However, due to the available evidence, as well as strong clinical support for surgical lead placement as an alternative to percutaneous test stimulation, surgical lead placement may be considered medically necessary for otherwise eligible patients.

The literature on sacral nerve stimulation for constipation or chronic pelvic pain remains insufficient to evaluate the effect of this technology on health outcomes; thus SNM is considered investigational for these indications.

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HCPCS	A4290, C1767, C1778, C1816, C1883, C1897, E0745, L8680, L8685, L8686, L8687, L8688
ICD-9 Diagnosis	787.60 thru 787.63, 788.20 thru 788.29, 788.30 thru 788.39
ICD-9 Procedure	04.92, 86.94

Policy History

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03/21/2002	Medical Policy Committee review
03/25/2002	Managed Care Advisory Council approval
06/24/2002	Format revision. No substance change to policy.
10/05/2004	Medical Director review
11/16/2004	Medical Policy Committee review. Format revision. Policy focus expanded to include other pelvic floor dysfunction conditions in addition to urinary incontinence.
11/29/2004	Managed Care Advisory Council approval
10/05/2005	Medical Director review
10/18/2005	Medical Policy Committee review. Format revision. FDA approval information added. Coverage eligibility unchanged.
10/27/2005	Quality Care Advisory Council approval
10/04/2006	Medical Director review
10/18/2006	Medical Policy Committee approval. Format revision; updated with additional references. Coverage eligibility unchanged.
09/05/2007	Medical Director review
09/19/2007	Medical Policy Committee approval. Coverage eligibility unchanged.
09/09/2008	Medical Director review
09/17/2008	Medical Policy Committee approval. Coverage eligibility unchanged. A note stating that a successful trial response to a peripheral nerve stimulation test is required prior to permanent placement under general anesthesia.
06/04/2009	Medical Director review
06/17/2009	Medical Policy Committee approval. Coverage eligibility unchanged.
06/03/2010	Medical Policy Committee approval

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06/16/2010 Medical Policy Implementation Committee approval. Added criteria for SNM for the treatment of patients with urge incontinence, urgency-frequency and non-obstructive urinary retention to be eligible for coverage as follows:
- The patient is an appropriate surgical candidate; and
- A successful percutaneous test stimulation, defined as at least 50% improvement in symptoms, was performed.

Change coverage for fecal incontinence from investigational to eligible for coverage with criteria.
06/02/2011 Medical Policy Committee review
06/15/2011 Medical Policy Implementation Committee approval. Format revision; including, addition of FDA and or other governmental regulatory approval and rationale/source. Coverage eligibility unchanged.
06/14/2012 Medical Policy Committee review
06/20/2012 Medical Policy Implementation Committee approval. No change to coverage.
06/06/2013 Medical Policy Committee review
06/25/2013 Medical Policy Implementation Committee approval. Title changed. “For Pelvic Floor” dropped. Criteria revised.
06/05/2014 Medical Policy Committee review
06/18/2014 Medical Policy Implementation Committee approval. No change to coverage.
Next Scheduled Review Date: 06/2015

*****Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
    2. credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. in accordance with nationally accepted standards of medical practice;
B. clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and 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.

For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

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