Percutaneous Tibial Nerve Stimulation

Policy Number: 7.01.106  Last Review: 5/2017

Policy
Blue Cross and Blue Shield of Kansas City (Blue KC) will not provide coverage for percutaneous tibial nerve stimulation. This is considered investigational.

Please note that this is a type of electrical stimulation that is considered a benefit exclusion in many health plan contracts.

When Policy Topic is covered
Not Applicable

When Policy Topic is not covered
Percutaneous tibial nerve stimulation is considered investigational for all indications, including but not limited to the following:
- Urinary dysfunction, including but not limited to overactive bladder syndrome, neurogenic bladder, urinary frequency, urgency, incontinence, and retention.
- Fecal incontinence.

Considerations
Note: There is no separate policy statement for patients with interstitial cystitis, as they would be considered candidates for PTNS therapy based on the presence of urgency and frequency alone.

Description of Procedure or Service

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<td>Interventions of interest are:</td>
<td>Comparators of interest are:</td>
<td>Relevant outcomes include:</td>
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Percutaneous tibial nerve stimulation (PTNS; also known as posterior tibial nerve stimulation) is a technique of electrical neuromodulation used primarily for treating voiding dysfunction.

The evidence for PTNS in individuals who have non-neurogenic urinary dysfunction including overactive bladder (OAB) includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. A number of RCTs have been published, including 2 key industry-sponsored RCTs, the OrBIT and SUmiT trials. Systematic reviews of the published trials have found short-term improvements with PTNS and have not identified long-term comparative studies. The largest, highest quality study was the double-blinded, sham-controlled SUmiT trial. It reported a statistically significant benefit of PTNS and sham at 12 weeks. Two other sham-controlled RCTs, including 1 published in 2015, had mixed findings on short-term efficacy of PTNS. The nonblinded OrBIT trial found that PTNS was noninferior to medication treatment at 12 weeks. Longer term comparative data are not available after the initial 12-week treatment period. Up to 36 months of uncontrolled data are available but only for patients enrolled in RCTs who responded to an initial course of treatment who may not be representative of the patient population as a whole. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for PTNS in individuals who have neurogenic bladder includes several RCTs and a systematic review of RCTs and observational data. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Only a few RCTs evaluating tibial nerve stimulation for treating neurogenic bladder have been published to date and all but 1 performed transcutaneous stimulation rather than PTNS. Studies varied widely in factors, such as the study population and comparison intervention. Study findings have not reported that tibial nerve stimulation significantly improved incontinence symptoms and other outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.
The evidence for PTNS in individuals who have fecal incontinence includes several RCTs and systematic reviews. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. The available RCTs have not found a clear benefit of PTNS. Neither of the sham-controlled trials found that active stimulation was superior to sham for achieving the primary outcome, at least a 50% reduction in mean weekly fecal incontinence episodes. The larger sham-controlled RCT did find a significantly greater decrease in absolute number of weekly incontinence episodes in the active treatment group, but the overall trial findings did not suggest superiority of PTNS over sham treatment. Systematic reviews have not conducted pooled analyses. The evidence is insufficient to determine the effects of the technology on health outcomes.

Background
Altering the function of the posterior tibial nerve with posterior tibial nerve stimulation (PTNS) is believed to improve voiding function and control. While the posterior tibial nerve is located near the ankle, it is derived from the lumbar-sacral nerves (L4-S3), which control the bladder detrusor and perineal floor. Voiding dysfunction includes urinary frequency, urgency, incontinence, and nonobstructive retention. Common causes of voiding dysfunction are pelvic floor dysfunction (e.g., from pregnancy, childbirth, surgery), inflammation, medication (e.g., diuretics and anticholinergics), obesity, psychogenic factors, and disease (e.g., multiple sclerosis, spinal cord injury, detrusor hyperreflexia, diabetes with peripheral nerve involvement). The current FDA-cleared indication for PTNS is overactive bladder (OAB), which is defined as the presence of urinary urgency, with or without urgency urinary incontinence, that is usually accompanied by frequency and nocturia and is not associated with urinary tract infections or other known pathology.

The procedure for PTNS consists of the insertion of a needle above the medial malleolus into the posterior tibial nerve followed by the application of low-voltage (10 mA, 1–10 Hz frequency) electrical stimulation that produces sensory and motor responses (i.e., a tickling sensation and plantar flexion or fanning of all toes). Noninvasive PTNS has also been delivered with surface electrodes. The recommended course of treatment is an initial series of 12 weekly office-based treatments followed by an individualized maintenance treatment schedule.

PTNS is less invasive than traditional sacral nerve neuromodulation (referenced in another policy), which has been successfully used in the treatment of urinary dysfunction but requires implantation of a permanent device. In sacral root neuromodulation, an implantable pulse generator that delivers controlled electrical impulses is attached to wire leads that connect to the sacral nerves, most commonly the S3 nerve root that modulates the neural pathways controlling bladder function.

PTNS is not cleared by FDA for treating fecal incontinence; however, the treatment has been proposed for this purpose. The manufacturer recommends a course of
treatment for fecal incontinence similar to the one used to treat OAB; an initial course of 12 weekly sessions of tibial nerve stimulation followed by a personalized schedule of follow-up treatments.

**Regulatory Status**
In July 2005, the Urgent® PC Neuromodulation System (Uroplasty Inc.) received 510(k) marketing clearance from FDA for percutaneous tibial nerve stimulation to treat patients suffering from urinary urgency, urinary frequency, and urge incontinence. In 2010, the cleared indication was changed to “overactive bladder (OAB) and associated symptoms of urinary urgency, urinary frequency, and urge incontinence.” The Urgent PC Neuromodulation System is not FDA-cleared for other indications, such as the treatment of fecal incontinence.

**Rationale**
This evidence review was originally created in 2006 and has been updated regularly with searches of the MEDLINE database. The most recent literature review was performed through November 30, 2015. Following is a summary of the key literature to date.

**Non-Neurogenic Urinary Incontinence Including Overactive Bladder**

**Systematic Reviews**
An updated TEC Assessment on percutaneous tibial nerve stimulation (PTNS) for treatment of voiding dysfunction was published in December 2013 and concluded that PTNS as treatment for voiding dysfunction meets the TEC criteria for treatment of voiding dysfunction. The Assessment included 6 randomized controlled trials (RCTs) and had the following conclusion:

Evidence from randomized placebo-controlled trials supports the clinical efficacy of PTNS applied in the standard 12-week regimen. No concurrently controlled evidence exists from a trial over longer periods of time in maintenance therapy. Although the lack of controlled evidence on maintenance PTNS raises concern whether short-term efficacy is maintained over the long term, the available 12- to 36-month evidence appears consistent with maintained efficacy in relieving symptoms of overactive bladder (OAB) and urinary voiding dysfunction. Adverse event rates, assuming accurate ascertainment, appear limited.

In 2012 and 2013, several other systematic reviews of the literature on PTNS for treating OAB were published. Only 1 of these systematic reviews, however, conducted pooled analyses of study results. This review, by Burton et al, conducted a pooled analysis of data from 4 trials (2 of which were abstracts) comparing PTNS with sham treatment. They found a significantly higher risk of successful treatment with PTNS (risk ratio [RR], 7.02; 95% confidence interval [CI], 1.69 to 29.17) compared with a control intervention. The confidence interval was wide, indicating a lack of precision in the pooled estimate. The SUmiT trial, discussed below, contributed 220 of 289 patients (76%) in the pooled analysis.
Also in 2012, the Agency for Healthcare Research and Quality (AHRQ) Effective Health Care Program published a comparative effectiveness review on the broader topic of nonsurgical treatments for urinary incontinence in adult women. The review identified 4 reports of RCTs comparing PTNS and no active treatment in patients with OAB. Two of the 4 articles reported 12-week results of the sham-controlled SUmiT trial; one of these included a subgroup of SUmiT participants and was only published as an abstract. The AHRQ report included a pooled analysis of data from 3 studies that found statistically significantly greater improvement in urinary incontinence in the PTNS group compared with the control group (RR=1.9; 95% CI, 1.1 to 3.2). This pooled analysis included a total of 405 patients; 220 in the SUmiT trial, 150 in the SUmiT trial subanalysis and 35 in a trial by Finazzi-Agro et al. A limit of the analysis in the AHRQ review was that the 150 patients in the SUmiT subanalysis were included twice. The AHRQ report did not discuss evidence on the efficacy of PTNS beyond 12 weeks.

Randomized Controlled Trials
A number of RCTs have been published on PTNS for OAB, including 2 key industry-sponsored ones, the OrBIT trial and the SUmiT trial. Three of the RCTs are sham controlled, and the other RCTs compare PTNS to an alternate treatment regimen.

Sham-Controlled RCTs
The SUmiT trial, the largest trial completed to date, was a sham-controlled RCT published by Peters et al in 2010. Before conducting the trial, the researchers performed a pilot study in healthy volunteers to determine the adequacy of a sham PTNS intervention. Findings were that 10 of 30 volunteers (33%) correctly identified the sham procedure. This percentage is below the 50% that could be expected by chance; the investigators concluded that the procedure was a feasible sham. The SUmiT trial included patients with OAB syndrome. Eligibility criteria included a score of at least 4 on the Overactive Bladder Questionnaire short form for urgency, self-reported bladder symptoms lasting at least 3 months, and having failed conservative care. Data were collected from 23 centers in the United States. A total of 220 patients were randomly assigned, 110 to the PTNS group and 110 to the sham group. Both groups received 12 weekly 30-minute intervention sessions. In the sham group, a blunt (placebo) instrument was used to simulate the location and sensation of needle electrode insertion in active treatment. An inactive PTNS surface electrode was used and also 2 active transcutaneous electrical nerve stimulation (TENS) surface electrodes. The TENS unit was used to deliver low-level sensation to simulate the PTNS intervention. The 12-week course of treatment was completed by 103 of 110 (94%) in the PTNS group and 105 of 110 (95%) in the sham group.

The primary study outcome was response to treatment based on a single-item global response assessment (GRA) variable at 13 weeks. Possible responses were that symptoms were markedly worse, moderately worse, mildly worse, the same, slightly improved, moderately improved, or markedly improved. The proportion of patients who responded to treatment based on the GRA (ie, answered that symptoms were moderately or markedly improved) was 60 of 110 (54.5%) in the
PTNS group and 23 of 110 (20.9%) in the sham group; this difference was statistically significant (p<0.001). Intention-to-treat (ITT) analysis was used for the primary end point only. Several secondary outcomes also favored the PTNS group. The mean (SD) reduction in a symptom severity score (a lower score indicates less severity) was 36.7 (21.5) in the PTNS group and 29.2 (20.0) in the sham group (p=0.01). Similarly, the mean (SD) reduction in a quality-of-life scale, the 36-Item Short-Form Health Survey (a higher score indicates higher quality of life), was 34.2 (21.3) in the PTNS group and 20.6 (20.6) in the sham group (p=0.006).

For the 4 voiding diary variables, there were statistically significant differences between groups favoring PTNS. The mean (SD) change from baseline in the number of voids per day was -2.4 (2.5) in the PTNS group and -1.5 (2.4) in the sham group (difference between groups, 0.9 voids/d; p=0.01). The mean (SD) change in nocturia episodes was -0.7 (1.2) in the PTNS group and -0.3 (1.4) in the sham group (difference between groups, 0.4 nighttime voids; p=0.04). The mean change in moderate-to-severe urgency per day was -3.7 in the PTNS group and -2.0 in the sham group (difference between groups, 1.7 episodes; p<0.001). Finally, the mean change in urge incontinence episodes was -1.3 in the PTNS group and -0.3 in the sham group (difference between groups, 1 episode/d; p<0.002). (Standard deviations were not reported for the latter 2 outcomes.)

A limitation of the SUmiT trial was that the primary outcome, the GRA, was a single-item subjective measure. For the more objective measures—the voiding diary variables—there was statistically significantly greater benefit with PTNS compared with sham treatment; however, the clinical significance of the difference between the PTNS and sham groups was unclear (eg, on average, there was 1 fewer episode of urge incontinence a day in the PTNS group).

Another limitation of the SUmiT trial, as was the case with the OrBIT trial, is that only short-term comparative data are available. Unlike medication that can be taken in the same manner on an ongoing basis, PTNS involves an initial 12-week course of treatment followed by maintenance therapy, which varies from the initial treatment course. To date, maintenance therapy has not been well defined.

A SUmiT extension study included only those patients who had been assigned to the PTNS group and initially responded to treatment. That is, the extension study did not collect additional follow-up data from patients in the PTNS group who failed to meet the 12-week primary effectiveness end point or from patients assigned to the sham-control group. Among the 110 patients assigned to the PTNS group, 60 were initial responders and 50 of these entered the extension study. Data were available on 34 patients at 24 months and 29 patients at 36 months. After enrolling in the extension study, patients underwent a 14-week transitional protocol consisting of 2 treatments with a 14-day interval, 2 treatments with a 21-day interval and then 1 treatment after another 28 days. Following this 14-week period, a personal treatment plan was developed for each patient. PTNS treatments were delivered based on the patient’s reporting of symptoms; patients knew that PTNS sessions were available to them as needed when their symptoms
increased. Between 6 and 36 months, patients received a median of 1.1 PTNS treatments per month. In a per-protocol analysis, compared with baseline, 28 of 29 patients (97%) who completed the 36-month follow-up met the primary efficacy end point of moderate or marked improvement in overall bladder symptoms on the GRA. In addition, compared with baseline, all voiding diary measures were significantly improved in this group of patients at every 6-month follow-up.

Two additional small RCTs were also sham-controlled and double-blind. In 2015, Boudaoud et al reported on 20 children with OAB who were randomized to 12 weeks of treatment with PTNS (n=11) or a sham intervention (n=9). At the end of the treatment period, there were no statistically significant differences between groups on outcomes, including the proportion of patients with “good” versus “poor” urinary scores (p=0.65). (A 13-point scale was used; a “poor score” was defined as a decrease of 3 or fewer points posttreatment and a “good” score was a decrease of 4 to 6 points.)

The 2010 study by Finazzi-Agro et al included 35 women who had urge incontinence and detrusor overactivity on urodynamic testing. Patients were randomly assigned to 30-minute PTNS sessions 3 times per week for 4 weeks (n=18) or sham treatment (n=17). One patient dropped out of the PTNS group and 2 dropped out of the sham group; analysis was not ITT. The primary outcome, percent responders at 4 weeks (defined as at least 50% reduction in incontinent episodes) was attained by 12 (71%) of 17 in the PTNS group and 0 (0%) of 15 in the sham group.

**Other RCTs**

The OrBIT trial is the largest RCT that was not sham-controlled. This trial was published in 2009 by Peters et al and was a nonblinded comparison of PTNS and extended-release tolterodine (Detrol LA) in women with OAB. The study included 100 patients (50 per group); more than 90% were women. Eligibility included symptoms of OAB, with at least 8 voids per 24 hours; the mean daily voids for those entering the study were 12.3. A total of 87 (87%) of the 100 patients completed the study, and voiding diary data were available for 84 patients: 41 (82%) of 50 in the PTNS group and 43 (86%) of 50 in the tolterodine group.

The primary outcome was the noninferiority of PTNS in the mean reduction in the number of voids per 24 hours after 12 weeks of treatment. Noninferiority was defined as no more than a 20% difference in the mean void reduction. Study findings showed noninferiority of PTNS based on results for 84 of the 100 patients (84%). The decrease in number (SD) of voids per day was 2.4 (4.0) in the PTNS group and 2.5 (3.9) in the tolterodine group.

The study also reported a number of secondary outcomes, and findings on these were mixed. There were no statistically significant differences in the PTNS and tolterodine groups for other symptoms recorded in the voiding diary, including mean change in episodes of nocturia (-0.7 and -0.6, respectively), episodes of moderate-to-severe urgency per day (-2.2 and -2.9, respectively), and episodes of
urge incontinence per day (-1.0 and -1.7, respectively). In other secondary outcomes, 35 (79.5%) of 44 patients in the PTNS group and 23 (54.8%) of 42 in the tolterodine group reported symptom improvement or cure. This difference was statistically significant (p=0.01), favoring the PTNS group. However, the proportion of patients reporting symptom improvement (excluding the 3 patients reporting that they were cured) did not differ significantly between groups, which was 34 (77.3%) of 44 of those receiving PTNS and 21 (50%) of 42 receiving tolterodine.

The OrBIT trial lacked blinding of patients and providers and also lacked comparative data beyond the end of the initial 12-week treatment period. Moreover, there was no sham or placebo group to mitigate the potential bias due to subjective outcomes. In addition, the authors did not clearly define criteria for “improvement” or “cure,” which was a key secondary outcome, and did not report the extent of compliance with medical therapy. Finally, different methods of data collection were used in the 2 groups (eg, for adverse event outcomes and possibly for other self-reported outcomes).

Longer term comparative data on the OrBIT trial are not available. In 2010, MacDiarmid et al reported 1-year follow-up data for patients from the OrBIT trial who had been assigned to the PTNS group and had responded to the initial course of treatment, defined as having reported symptom improvement at 12 weeks. 14 Thirty-three of the 35 responders were included. They received a mean (SD) of 12.1 (4.9) additional treatments between the 12-week and 12-month visits, and there was a median of 17 days between treatments. Data were available for 32 (97%) of the 33 participants at 6 months and 25 (76%) of the 33 participants at 12 months. The mean (SD) reduction in number of voids per day from baseline (the original primary outcome of the study) was 3.2 (3.7) at 6 months and 2.8 (3.7) at 12 months. Other voiding diary outcomes at 12 months, based on 25 responses, were mean changes in nocturia episodes of -0.8, in episodes of moderate-to-severe urgency per day of -3.7, and in episodes of urge incontinence per day of -1.6.

As noted above, this analysis was limited in that no data from the tolterodine group were available to compare long-term outcomes. Additionally, not all patients in the PTNS group were included in the follow-up analysis; rather, only PTNS responders were eligible. A potential bias is that the initial subjective outcome measure may be subject to the placebo effect. Moreover, patients in the PTNS group who responded to initial treatment may be particularly susceptible to a placebo response and/or may represent those with the best treatment response. Thus, these individuals may also be susceptible to a placebo response during maintenance treatments, especially treatments offered on an as-needed basis.

The remaining RCTs compared PTNS to an alternative treatment, medication, conservative therapy, or electrical stimulation (ES). 7,12,15-18 The trials had mixed findings on short-term efficacy and none reported on the efficacy of PTNS beyond 12 weeks.
Two studies used medication treatment as the comparison intervention. In 2015, Preyer et al published a nonblinded study comparing 12 weeks of PTNS versus tolterodine in 36 women with OAB. Posttreatment, there were no significant differences between groups on the reduction of incontinence episodes in 24 hours (p=0.89) or quality of life (p=0.07).

Another RCT comparing PTNS to medication—in this case oral solifenacin—was a crossover trial published in 2013 by Vecchioli-Scaldazza et al. Forty women with OAB received PTNS (twice weekly for 6 weeks) and medication, given in random order, with a 6-week washout period between treatments. Group A received medication first and group B received PTNS first. The primary efficacy outcome was reduction in the number of voids in a 24-hour period. Thirty of the 40 patients (75%) completed the study. The number of daily voids (the primary outcome) significantly decreased after each treatment compared with before treatment. In addition, secondary outcomes including nocturia urge incontinence and voided volume, significantly improved after each treatment compared with pretreatment values. The authors did not directly compare the efficacy of medication and PTNS.

One RCT in Brazil compared PTNS to conservative therapy. The trial was published in 2010 by Schreiner et al and it included 51 women older than 60 years of age who complained of urge urinary incontinence. Women were randomized to 12 weeks of conservative treatment (Kegel exercises, bladder training) alone (n=26) or conservative treatment plus 12 weekly sessions of PTNS (n=25). Blinding was not discussed. The response rate at 12 weeks, defined as a reduction of at least 50% in the number of incontinence episodes reported by the patient in a bladder diary, was 76% in the PTNS group and 27% in the conservative treatment–only group (p=0.001).

Finally, a 2013 trial by Gungor Ugurlucan et al in Turkey compared transvaginal ES (n=38) and PTNS (n=21) in women with OAB. The ES protocol consisted of 20-minute treatments 3 times a week for 6 to 8 weeks. PTNS was performed with an Urgent PC device used for twelve 30-minute weekly sessions. A total of 52 (88%) of 59 patients completed the study. The authors assessed numerous outcome variables and did not specify primary outcomes or adjust p values for multiple comparisons. Four bladder diary variables were reported. From baseline to the end of the treatment period, the groups did not differ significantly at the p less than 0.05 level in mean change in urgency episodes, nocturia, or incontinence episodes. For example, the mean number (SD) of urgency episodes was 2.9 (4.1) at baseline and 1.6 (0.5) after treatment in the ES group and 2.0 (3.1) at baseline and 1.3 (0.5) after treatment in the PTNS group (p=0.54). There was a statistically significant difference in daytime frequency. The mean (SD) daytime frequency was 7.8 (2.7) at baseline and 5.8 (1.9) after treatment in the ES group and 7.6 (2.6) at baseline and 7.4 (2.9) in the PTNS group (p=0.03). The authors reported that a significantly higher proportion of patients in the ES group described themselves as cured, but they did not provide proportions or p values.
Section Summary: PTNS for Treating Non-Neurogenic Urinary Incontinence and OAB
A number of RCTs have been published, including 2 key industry-sponsored RCTs, the OrBIT and SUmiT trials. Systematic reviews of the evidence have found short-term improvements with PTNS and have not identified long-term comparative studies. The largest, highest quality study was the blinded sham-controlled SUmiT trial. This trial reported a statistically significant benefit of PTNS versus sham at 12 weeks. Two other small sham-controlled RCTs, including 1 published in 2015, had mixed findings on short-term efficacy of PTNS. The nonblinded OrBIT trial found that PTNS was noninferior to medication treatment at 12 weeks. No longer term comparative data are available after the initial 12-week treatment period. Up to 36 months of uncontrolled data are available for some patients enrolled in RCTs who responded to an initial course of treatment, but this subset of patients may not be representative of the entire study sample since it preferentially includes those with the best treatment response. This long-term uncontrolled data also does not control for a possible placebo effect and does not evaluate a uniform regimen of maintenance PTNS. As a result, the optimal maintenance regimen remains unclear.

Neurogenic Bladder Dysfunction
In 2015, Schneider et al published a systematic review of literature on tibial nerve stimulation (transcutaneous and percutaneous) for treating neurogenic lower urinary tract dysfunction. 19 Sixteen studies were identified—4 RCTs, 9 prospective cohort studies, 2 retrospective case series, and 1 case report. Sample sizes of the included studies were generally small; most included fewer than 50 patients and none had a sample size larger than 100 patients. Three of the 4 RCTs used transcutaneous tibial nerve stimulation and the fourth study, which was conducted in Iran, stated that PTNS was used but did not specify the device. The 4 RCTs included different study populations: women with neurogenic bladder (n=1), men with neurogenic overactive bladder (n=1), multiple sclerosis patients (n=1), and Parkinson disease patients (n=1). Comparison interventions were tolterodine, pelvic floor muscle training, lower-limb stretching, and sham (1 study each). Pooled analyses were not conducted and the systematic review mainly discussed intermediate outcomes (eg, maximum cystometric capacity, maximum detrusor pressure). In the articles reporting on RCT results, 20-23 none reported statistically significant between-group differences in clinical outcome variables (eg, number of episodes of urgency, frequency, nocturia).

Section Summary: PTNS for Treating Neurogenic Bladder Dysfunction
Few RCTs evaluating tibial nerve stimulation for treating neurogenic bladder have been published to date and all but 1 performed transcutaneous stimulation rather than PTNS. Studies varied widely in factors such as the study population and comparison intervention. Study findings have not suggested that tibial nerve stimulation significantly improved incontinence symptoms and other outcomes.

Fecal Incontinence
The Urgent PC Neuromodulation System is not FDA-cleared for the treatment of fecal incontinence. The company’s website states that the treatment can be used
for this condition and that the recommended initial course of treatment includes 12 weekly sessions.

Two systematic reviews of literature on tibial nerve stimulation for fecal incontinence have been published; neither conducted pooled analyses of PTNS outcomes compared with a sham or alternative intervention. Two systematic reviews of literature on tibial nerve stimulation for fecal incontinence have been published; neither conducted pooled analyses of PTNS outcomes compared with a sham or alternative intervention. Most recently, in 2015, Edenfeld et al identified 17 studies consisting of 13 case series and 4 RCTs. Three of the RCTs evaluated TENS stimulation and 1 used PTNS. A 2014 systematic review by Horrocks et al identified the same RCT, George et al, 2013 (described in more detail later) and also an RCT comparing PTNS with transcutaneous tibial nerve stimulation (TTNS). Horrocks identified 5 case series and 1 RCT that reported the outcome of 50% or greater reduction in the number of fecal incontinence episodes per week immediately after treatment. In these studies, a median of 71% of patients (range, 63%-82%) reported at least a 50% reduction in episodes. The Horrocks analysis is limited because it lacks a control group.

As of December 2015, 2 sham-controlled RCTs and 1 RCT comparing PTNS to sacral nerve stimulation (SNS) were identified. The first sham-controlled study was published in 2013 by George et al in the U.K. Thirty patients (28 women) who had failed conservative therapy for fecal incontinence were randomized to PTNS (n=11), TTNS (n=11), or sham transcutaneous stimulation (n=8). Patients in all groups received a total of 12 treatments given twice-weekly for 6 weeks. (This differs from the PTNS manufacturer’s recommended course of 12 weekly treatments.) The primary study end point was at least a 50% reduction in the mean number of incontinence episodes per week at the end of the 6-week treatment period. Only 1 patient did not complete the study, and data were analyzed on an ITT basis. Nine of 11 patients in the PTNS group, 5 of 11 in the TTNS group, and 1 of 8 in the sham group attained the primary end point; the difference among groups was not statistically significant (p=0.035). All of the responders reported no weekly episodes of fecal incontinence after treatment; however, these findings are limited by the small sample size and short-term follow-up.

A larger sham-controlled RCT, known as the CONFIDeNT trial, was published in 2015 by Knowles et al in the U.K. The study was double-blind and multicenter. A total of 227 patients with fecal incontinence sufficiently severe to warrant intervention (according to the principal investigator at each site) were randomized to receive PTNS (n=115) or sham stimulation (n=112). Both groups received 12 weekly intervention sessions lasting 30 minutes each. The primary outcome was at least a 50% reduction in the mean number of episodes of fecal incontinence per week compared with baseline. The mean number of episodes was calculated from 2-week bowel diaries. Twelve patients withdrew from the study. After treatment, 39 (38%) of 103 in the PTNS group and 32 (31%) of 102 in the sham group had at least a 50% reduction in the number of fecal incontinence episodes per week. The difference between groups was not statistically significant (adjusted odds ratio, 1.28; 95% CI, 0.72 to 2.28; p=0.396). There were also no significant differences between the PTNS and sham groups in the proportion of patients...
achieving more than 25%, more than 75%, or 100% reduction in mean weekly episodes. There was, however, a significantly greater reduction in the absolute mean number of weekly fecal incontinence episodes in the active PTNS group. The mean number of weekly fecal incontinence episodes in the PTNS group was 6.0 at baseline and 3.5 after treatment. This compares to means of 6.9 and 4.8, respectively, in the sham group. The difference between groups was -2.26 (95% CI, -4.18 to -0.35; p=0.021).

In 2015, Thin et al published data on PTNS versus SNS for fecal incontinence.²⁸ A total of 40 women were randomized, 17 to PTNS and 23 to SNS. Patients in the PTNS group had an initial course of 12 weekly sessions, and also received 3 maintenance treatments during the following 2 months. SNS was provided using a 2-stage approach; in particular, test stimulation followed by permanent stimulation if they achieved a decrease in fecal incontinence episodes of at least 50% over the 2-week test period. The primary outcome was a reduction of at least 50% in fecal incontinence episodes per week (as determined by 2-week bowel diaries). Fifteen women passed temporary SNS and underwent permanent implantation. The proportion of patients who achieved the primary outcome at 6 months was 11 (61%) of 18 in the SNS group and 7 (47%) of 15 in the PTNS group. Proportions at 3 months were 9 (47%) of 19 in the SNS group and 6 (38%) of 16 in the PTNS group. The authors noted that because this was a pilot study, direct statistical comparison of SNS and PTNS was not conducted.

**Section Summary: PTNS for Treating Fecal Incontinence**
Few RCTs evaluating PTNS for the treatment of fecal incontinence have been published to date. The available RCTs have not found a clear benefit of PTNS. Neither of the sham-controlled trials found that active stimulation was superior to sham for achieving the primary outcome of at least a 50% reduction in mean incontinence episodes. The larger sham-controlled RCT did find a significantly greater decrease in absolute number of weekly incontinence episodes in the active treatment group, but the overall trial findings did not suggest superiority of PTNS over sham treatment. Systematic reviews have not conducted pooled analyses.

**Ongoing and Unpublished Clinical Trials**
Some currently unpublished trials that might influence this review are listed in Table 1.

**Table 1. Summary of Key Trials**

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NCT: national clinical trial.

**Summary of Evidence**
The evidence for percutaneous tibial nerve stimulation (PTNS) in individuals who have non-neurogenic urinary dysfunction including overactive bladder (OAB)
includes randomized controlled trials (RCTs) and systematic reviews. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. A number of RCTs have been published, including 2 key industry-sponsored RCTs, the OrBIT and SUmiT trials. Systematic reviews of the published trials have found short-term improvements with PTNS and have not identified long-term comparative studies. The largest, highest quality study was the double-blinded, sham-controlled SUmiT trial. It reported a statistically significant benefit of PTNS and sham at 12 weeks. Two other sham-controlled RCTs, including 1 published in 2015, had mixed findings on short-term efficacy of PTNS. The nonblinded OrBIT trial found that PTNS was noninferior to medication treatment at 12 weeks. Longer term comparative data are not available after the initial 12-week treatment period. Up to 36 months of uncontrolled data are available but only for patients enrolled in RCTs who responded to an initial course of treatment who may not be representative of the patient population as a whole. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for PTNS in individuals who have neurogenic bladder includes several RCTs and a systematic review of RCTs and observational data. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. Only a few RCTs evaluating tibial nerve stimulation for treating neurogenic bladder have been published to date and all but 1 performed transcutaneous stimulation rather than PTNS. Studies varied widely in factors, such as the study population and comparison intervention. Study findings have not reported that tibial nerve stimulation significantly improved incontinence symptoms and other outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for PTNS in individuals who have fecal incontinence includes several RCTs and systematic reviews. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. The available RCTs have not found a clear benefit of PTNS. Neither of the sham-controlled trials found that active stimulation was superior to sham for achieving the primary outcome, at least a 50% reduction in mean weekly fecal incontinence episodes. The larger sham-controlled RCT did find a significantly greater decrease in absolute number of weekly incontinence episodes in the active treatment group, but the overall trial findings did not suggest superiority of PTNS over sham treatment. Systematic reviews have not conducted pooled analyses. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical Input Received From Physician Specialty Societies and Academic Medical Centers
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.
In response to requests, input was received through 3 physician specialty societies and 1 academic medical center while this policy was under review in 2012. Clinical input was mixed. There was no consensus or near-consensus that the policy should be changed. The range of opinions included that PTNS should be considered investigational, that it should be considered for use in medically refractory patients as second-line treatment, and that the evidence is sufficient to consider this treatment to be medically necessary.

**Practice Guidelines and Position Statements**

**American Urological Association et al**

In 2014, the American Urological Association and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction published a guideline on diagnosis and treatment of non-neurogenic overactive bladder in adults.\(^{29,30}\) The guideline included a statement that clinicians may offer PTNS as a third-line treatment option in carefully selected patients. The statement was rated as grade C, indicating that the balance of benefits and risks/burdens are uncertain. (This is a revised version of a 2012 guideline; the statement on PTNS did not change).

**American College of Obstetricians and Gynecologists**

The 2015 American College of Obstetricians and Gynecologists practice bulletin on treatment of urinary incontinence in women did not address PTNS or other types of nerve stimulation.\(^{31}\)

**U.S. Preventive Services Task Force Recommendations**

Not applicable.

**Medicare National Coverage**

There is no national coverage determination (NCD). In the absence of an NCD, coverage decisions are left to the discretion of local Medicare carriers.

References


**Billing Coding/Physician Documentation Information**

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<th>Code</th>
<th>Description</th>
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<tbody>
<tr>
<td>64566</td>
<td>Posterior tibial neurostimulation, percutaneous needle electrode, single treatment, includes programming</td>
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<tr>
<td>64999</td>
<td>Unlisted procedure, nervous system</td>
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<tr>
<td>97014</td>
<td>Application of a modality to 1 or more areas; electrical stimulation (unattended)</td>
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<tr>
<td>97032</td>
<td>Application of a modality to 1 or more areas; electrical stimulation (manual), each 15 minutes</td>
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<tr>
<td>L8679</td>
<td>Implantable neurostimulator, pulse generator, any type</td>
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**ICD10 Codes**

- **N32.81** Overactive bladder
- **N39.41- N39.498** Other specified urinary incontinence code range
- **R33.0- R33.9** Retention of urine code range
- **R35.0** Frequency of micturition
- **R39.15** Urgency of urination

Prior to 2011, the correct CPT code to use for PTNS needle insertion is the unlisted CPT code 64999. CPT codes for percutaneous implantation of neurostimulator electrodes (i.e., 64553-64565) are not appropriate since PTNS uses percutaneously inserted needles and wires rather than percutaneously implanted electrodes. The stimulation devices used in PTNS and PNT are not implanted, so CPT code 64590 is also not appropriate.

**Additional Policy Key Words**

N/A
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<tr>
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