Percutaneous Tibial Nerve Stimulation

Policy # 00415
Original Effective Date: 04/16/2014
Current Effective Date: 06/20/2018

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.

Note: Botulinum Toxins is addressed separately in medical policy 00012.

Note: Injectable Bulking Agents for the Treatment of Urinary and Fecal Incontinence is addressed separately in medical policy 00095.

Note: Sacral Nerve Neuromodulation/Stimulation is addressed separately in medical policy 00108.

Note: Percutaneous Electrical Nerve Stimulation (PENS) and Percutaneous Neuromodulation Therapy (PNT) is addressed separately in medical policy 00144.

Note: Transanal Radiofrequency Treatment of Fecal Incontinence is addressed separately in medical policy 00571.

When Services Are 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.*

Based on review of available data, the Company may consider maintenance therapy using monthly PTNS for individuals following a 12-week initial course of PTNS that resulted in improved urinary dysfunction meeting treatment goals to be **eligible for coverage.**

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.*

Based on review of available data, the Company may consider posterior tibial nerve stimulation (PTNS) for an initial 12-week course for individuals with non-neurogenic urinary dysfunction including overactive bladder (OAB) symptoms present for at least 3 months to be **eligible for coverage.**

Patient Selection Criteria
Coverage eligibility will be considered for PTNS for an initial 12-week course for individuals with non-neurogenic urinary dysfunction including OAB symptoms present for at least 3 months if both criteria are met:

- Failed behavioral therapy following an appropriate duration of 8 to 12 weeks without meeting treatment goals; and
- Failed pharmacologic therapy, e.g., oral anti-muscarinics and/or transdermal oxybutynin, following 4 to 8 weeks of treatment without meeting treatment goals.

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 the use of PTNS when patient selection criteria are not met to be **investigational.***

Based on review of available data, the Company considers PTNS for all other indications, to be **investigational**, including but not limited to the following.*****

- Neurogenic bladder dysfunction
- Fecal incontinence.

Policy Guidelines

Patients may be considered to have failed behavioral therapies following an appropriate duration of 8 to 12 weeks without meeting treatment goals (Gormley et al [2015]).

Patients may be considered to have failed pharmacologic therapies following 4 to 8 weeks of treatment without meeting treatment goals (Gormley et al [2015]).

Annual evaluation by a physician may be performed to ensure efficacy is continuing for maintenance PTNS treatments.

Background/Overview

VOIDING DYSFUNCTION

Common causes of voiding dysfunction are pelvic floor neuromuscular changes (e.g., from pregnancy, childbirth, surgery), inflammation, medication (e.g., diuretics, anticholinergics), obesity, psychogenic factors, and disease (e.g., multiple sclerosis, spinal cord injury, detrusor hyperreflexia, diabetes with peripheral nerve involvement).

Altering the function of the posterior tibial nerve with PTNS is believed to improve voiding function and control. The mechanism of action is believed to be retrograde stimulation of the lumbosacral nerves (L4-S3) via the posterior tibial nerve located near the ankle. The lumbosacral nerves control the bladder detrusor and perineal floor. OAB is voiding dysfunction that is characterized by urinary frequency, urgency, urge incontinence, and nonobstructive retention.

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

The current indication cleared by the U.S. FDA for PTNS is OAB and associated symptoms of urinary frequency, urinary urgency, and urge incontinence.

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 as evidenced by a tickling sensation and plantarflexion or fanning of all toes. Noninvasive PTNS has also been delivered with transcutaneous or 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 (see medical policy 00108), 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 has been proposed as a treatment for non-neurogenic and neurogenic bladder syndromes and fecal incontinence.

FDA or Other Governmental Regulatory Approval

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

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

There is developing wireless technology for the treatment of OAB, approved in Europe. BlueWind (BlueWind Medical) is a wireless, battery-less, miniature implantable neurostimulator that is activated by an external device worn at the ankle.

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

Device Name	Manufacturer	Cleared	510(k)	Indications
Urgent® PC Neuromodulation System	Uroplasty, now Cogentix Medical	Oct 2005	K052025	Indicated for treatment of urinary urgency, urinary frequency, and urge incontinence
Urgent® PC Neuromodulation System	Uroplasty, now Cogentix Medical	Jul 2006	K061333	FDA determined the 70% isopropyl alcohol prep pad contained in the kit is subject to regulation as a drug
Urgent® PC Neuromodulation System	Uroplasty, now Cogentix Medical	Aug 2007	K071822	Labeling update, intended use is unchanged
Urgent® PC Neuromodulation System	Uroplasty, now Cogentix Medical	Oct 2010	K101847	Intended use statement adds the diagnosis of overactive bladder
NURO™ Neuromodulation System	Advanced Uro-Solutions, now Medtronic	Nov 2013	K132561	Intended to treat patients with overactive bladder and associated symptoms of urinary urgency, urinary frequency, and urge incontinence

FDA: Food and Drug Administration.

Centers for Medicare and Medicaid Services (CMS)
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Rationale/Source

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.

NON-NEUROGENIC URINARY DYSFUNCTION INCLUDING OVERACTIVE BLADDER
For this section, the clinical context includes 2 related clinical indications, where the population for the second indication is a subset of the first population: (1) individuals with non-neurogenic urinary dysfunction including OAB who have failed behavioral and pharmacologic therapy and are treated with an initial course of PTNS; and (2) individuals with OAB syndrome responsive to an initial course of PTNS who are treated

with maintenance PTNS. The evidence review is combined for both indications, although the section summary provides specific evidence conclusions for each clinical indication.

This review was informed a TEC Assessment (2013) on PTNS for treatment of voiding dysfunction. It concluded that PTNS as a treatment for voiding dysfunction met TEC criteria and showed that PTNS improves the net health outcome. PTNS ameliorates symptoms of chronic OAB or urinary voiding dysfunction, simultaneously improving quality of life parameters among patients who have failed behavioral and pharmacologic therapies.

The Assessment evaluated 6 RCTs and drew the following conclusion about the evidence:

"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 OAB and urinary voiding dysfunction. Adverse event rates, assuming accurate ascertainment, appear limited."

The following summarizes key RCTs reviewed in the TEC Assessment.

Sham-Controlled Randomized Trials
The Sham Effectiveness in Treatment of Overactive Bladder Symptoms (SUmiT) trial was a sham-controlled randomized trial published by Peters et al (2010). Before conducting the trial, investigators performed a pilot study in healthy volunteers to determine the adequacy of a sham PTNS intervention. The sham procedure was correctly identified by 10 (33%) of 30 volunteers. This percentage is below the 50% that could be expected by chance, and the investigators concluded that the procedure was a feasible sham. 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 for these symptoms or a diagnosis of OAB. OAB and quality of life questionnaires, as well as 3-day voiding diaries, were completed at baseline and 13 weeks.

Both the randomized sham and active intervention 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. One inactive PTNS surface electrode and 2 active transcutaneous electrical nerve stimulation surface electrodes were used. The transcutaneous electrical nerve stimulation unit (Urgent PC system) delivered low-level stimulation to simulate the PTNS intervention. The 12-week treatment was completed by 103 (94%) of 110 in the PTNS group and 105 (95%) of 110 in the sham group.

The primary end point of this trial was the assessment of the efficacy of PTNS compared with an inactive sham intervention in subjects who had overall OAB symptoms. Analysis was done by intention-to-treat. A responder was defined as one reporting bladder symptoms as moderately or markedly improved on a 7-

level global response assessment (GRA) tool at week 13. Possible responses were that symptoms were markedly worse, moderately worse, mildly worse, the same, slightly improved, moderately improved, or markedly improved. The primary end point of a GRA response of moderately to markedly improved overall bladder symptoms was achieved in 54.5% (60/110) of PTNS subjects compared with 20.9% (23 of 110) of sham subjects. There was a statistically significantly greater benefit reported with PTNS than with sham treatment in voiding diary variables.

Six PTNS subjects reported 9 mild or moderate treatment-related adverse events consisting of ankle bruising, discomfort at the site of needle insertion, bleeding at the site, and tingling in the leg. No local treatment-related adverse events were reported in the sham group, and no systemic adverse events occurred in either group.

The Sustained Therapeutic Effects of Percutaneous Tibial Nerve Stimulation (STEP) trial, an extension of the SUmiT study, included only those patients assigned to the PTNS group with initially responded to treatment. The purpose was to determine the threshold for continued treatment to consider potential maintenance therapy. Of the 60 PTNS group 13-week responders, 50 entered the extension study. 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 was 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 after the 14-week tapering period. Data were available on 34 patients at 24 months and on 29 patients at 36 months. In a per-protocol analysis, compared with baseline, 28 (97%) of 29 patients 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. Also, compared with baseline, all voiding diary measures were significantly improved in this group of patients at every 6-month follow-up.

Adverse events noted in the STEP study included 1 report of restricted vaginal opening with unknown relation to treatment, and 2 mild bleeding events at the needle site were reported in the same participant. Nine patients reported 11 mild adverse events with an unknown relation to treatment including vaginal bleeding, mild depression, shoulder pain, diarrhea, leg pain, stomach ache, pelvic pain, urinary tract infection, a pulling sensation in both feet, bladder pressure, and pinched nerve pain.

A limitation of the SUmiT trial was that the primary outcome (the GRA) was a single-item subjective measure. An additional limitation of the SUmiT trial was 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.

The SUmiT RCT and STEP extension study are summarized in Tables 2 and 3.

Table 2. Summary of SUmiT RCT and STEP Extension Characteristics

Study (Trial)	Countries	Sites	Dates	Randomized or Enrolled/ Completed Trial		Outcome
				PTNS	Sham	
Peters et al (2010) (SUmiT)	U.S.	23	2008-2009	110/103	110/105	GRA at 13 wk
Peters et al (2013) (STEP)	U.S.	23	2009-2012	50/29[a]	None	GRA at 36 mo

GRA: global response assessment; PTNS: percutaneous tibial nerve stimulation; RCT: randomized controlled trial; STEP: Sustained Therapeutic Effects of Percutaneous Tibial Nerve Stimulation; SUmiT: Sham Effectiveness in Treatment of Overactive Bladder Symptoms.
[a] Extension study of 50 PTNS responders in SUmiT trial.

Table 3. Summary of SUmiT RCT and STEP Extension Results

Study	Primary Outcome: Moderately or Markedly Improved GRA			
	PTNS, n/N (%)	Sham, n/N (%)	Confidence Intervals	p
SUmiT (2010)				
GRA (13 wk)	60/110 (54.5)	23/110 (20.9)	NR	<0.001
STEP (2013)				
GRA (36 mo)	28/29 (97)	None	None	None

GRA: Global response assessment; NR: not reported; PTNS: percutaneous tibial nerve stimulation; RCT: randomized controlled trial; STEP: Sustained Therapeutic Effects of Percutaneous Tibial Nerve Stimulation: SUmiT: Sham Effectiveness in Treatment of Overactive Bladder Symptoms.

Study	Countries	Sites	Dates	Randomized/Completed		Outcome[a] Reduction in Voids
				PTNS	Tolterodine	
Peters et al (2009)	U.S.	11	2006-2008	50/41	50/43	Reported
MacDiarmid et al (2010) 1-y follow-up	U.S.	11	2008-2009	33/32[b]		Reported

OrBIT: Overactive Bladder Innovative Therapy, PTNS: percutaneous tibial nerve stimulation; RCT: randomized controlled trial.
[a] Mean reduction in the number of voids per 24 hours after 12 weeks of treatment.
[b] Eligible responders from 12-week study.

Table 5. Summary of OrBIT RCT Results

Study	Primary Outcome: Mean Reduction in Voids per Day (SD)			
OrBIT (2009)	PTNS (n=41)		Tolterodine (n=43)	
	Baseline	12 Weeks	Baseline	12 Weeks
Voids per day	12.1 (3.1)	-2.4 (4.0)	12.5 (3.7)	-2.5 (3.9)
p		<0.001		<0.001
Confidence interval		NR		NR
OrBIT 1-y follow-up (2010)[7]	PTNS (n=25)			
	Baseline	12 Months		
Voids per day	12.4 (3.5)	-2.8 (3.7)	Not applicable	Not applicable
p		<0.001		
Confidence interval		NR		

NR: not reported; OrBIT: Overactive Bladder Innovative Therapy, PTNS: percutaneous tibial nerve stimulation; RCT: randomized controlled trial.

Additional RCTs not included in the Technology Evaluation Center (TEC) Assessment or published since 2013 are reviewed next.

This group of RCTs compared PTNS with an alternative treatment, medication, conservative therapy, or electrical stimulation. The trials had mixed findings on short-term efficacy, and none reported on the efficacy of PTNS beyond 12 weeks.

Two studies used medication as the comparison intervention. Preyer et al (2015) published a nonblinded study comparing 12 weeks of PTNS with tolterodine in 36 women who had OAB. Post-treatment, 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 with medication—in this case, oral solifenacin—was a crossover trial published by Vecchioli-Scaldazza et al (2013). Forty women with OAB received PTNS (twice weekly for 6 weeks) or 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 a reduction in the number of voids in a 24-hour period. Thirty (75%) of the 40 patients completed the trial. The number of daily voids (the primary outcome) significantly decreased after each treatment compared with before treatment. Also, 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 with PTNS.

One RCT in Brazil compared PTNS with conservative therapy. The trial, reported by Schreiner et al (2010), 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 trial by Gungor Ugurlucan et al (2013) in Turkey compared transvaginal electrical stimulation (n=38) with PTNS (n=21) in women who had OAB. The electrical stimulation 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. Fifty-two (88%) of 59 patients completed the trial. 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 of urgency episodes was 2.9 at baseline and 1.6 after treatment in the electrical stimulation group, and 2.0 at baseline and 1.3 after treatment in the PTNS group (p=0.54). There was a statistically significant difference in daytime frequency. The mean daytime frequency was 7.8 at baseline and 5.8 after treatment in the electrical stimulation group, and 7.6 at baseline and 7.4 in the PTNS group (p=0.03). The authors reported that a significantly higher

proportion of patients in the electrical stimulation group described themselves as cured, but they did not provide proportions or p values.

Systematic Reviews
In 2012 and 2013, several other systematic reviews of the literature on PTNS for treating OAB were published. Only one of them, however, conducted pooled analyses of study results. This review, by Burton et al (2012), conducted a pooled analysis of data from 4 trials (two of which were abstracts) comparing PTNS with sham treatment. Reviewers found a significantly higher risk of successful treatment with PTNS (relative risk, 7.02; 95% confidence interval [CI], 1.69 to 29.17) compared with a control intervention. The CI was wide, indicating a lack of precision in the pooled estimate. The patient samples in these studies were homogenous by sex, severity and duration of symptoms, and previous treatment history. The definition of successful treatment also varied among studies. The SUmiT trial (discussed above) contributed 220 (76%) of 289 patients in the pooled analysis.

Also in 2012, the Agency for Healthcare Research and Quality (AHRQ) published a comparative effectiveness review on the broader topic of nonsurgical treatments for urinary incontinence in adult women. Reviewers identified 4 reports of RCTs comparing PTNS with no active treatment in patients with OAB. Two of the 4 articles reported on 12-week results of the sham-controlled SUmiT trial; one of them 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 than in the control group (relative risk, 1.9; 95% CI, 1.1 to 3.2). This pooled analysis included 405 patients: 220 in the SUmiT trial, 150 in the SUmiT trial subgroup analysis, and 35 in a trial by Finazzi-Agro et al (2010). A limit of the AHRQ analysis was that the 150 patients in the SUmiT subgroup analysis were included twice. The AHRQ report did not discuss evidence on the efficacy of PTNS beyond 12 weeks.

A Cochrane review by Stewart et al (2016) evaluated electrical stimulation with nonimplanted electrodes for OAB in adults. The literature search was current up to December 2015. The objective of the review was to determine whether electrical stimulation (including PTNS) was better than no treatment or better than any other treatment available for OAB. PTNS and other forms of electrical stimulation including nonimplanted devices were reviewed to determine which resulted in better outcomes for OAB and associated adverse events. Studies reviewed were RCTs or quasi-RCTs of electrical stimulation that included adults with OAB with or without urgency and urge urinary incontinence. Trials whose participants had stress urinary incontinence were excluded. Sixty-three eligible trials were identified (total N=4424 randomized participants). The Cochrane review included several trials assessed herein: the OrBIT (Peters) and OrBIT follow-up (MacDiarmid) trials, SUmiT (Peters) trial, STEP (Peters) trial, and the Finazzi-Agro, Schreiner, Vecchioli-Scaldazza, and Preyer trials.

Data were obtained from the end of treatment and the longest available follow-up period. The primary outcomes were identified as the perception of cure, the perception of improvement, and condition-related quality of life measures as defined by the original authors or by any validated measurement scales such as

the International Consultation on Incontinence Questionnaire. Secondary outcomes pertinent to the evidence review were a quantification of symptoms, procedure outcome measures, and adverse effects. The key findings from the Cochrane review (2016) of evidence are summarized in Table 6.

Table 6. Summary of Systematic Review Outcomes

ES Effect	Outcomes	Comparators	QOE
More effective[a]	Improvement in OAB symptoms, UUI and OAB-related QOL	No active treatment, placebo, or sham	Moderate
More effective	Improvement in OAB symptoms	PFMT	Moderate
More effective	Improvement in OAB symptoms	Drug therapy	Moderate
Effect uncertain	Improvement in UUI	PFMT	No evidence
Effect uncertain	Improvement in UUI	Drug therapy	No evidence
Effect uncertain	Improvement in OAB-related QOL	PFMT	Low
Effect uncertain	Improvement in OAB-related QOL	Drug therapy	No evidence
Lower risk	Adverse events	Oxybutynin or tolterodine	Low
Lower risk	Adverse events	Placebo/sham	Moderate

Adapted from Stewart et al (2016).
ES: electrical stimulation (includes percutaneous tibial nerve stimulation); OAB: overactive bladder; PFMT: pelvic floor muscle training; QOE: quality of evidence; QOL: quality of life; UUI: urge urinary incontinence.
[a] "While both intravaginal ES and percutaneous tibial nerve stimulation are likely to lead to greater improvement in symptoms than sham/placebo, intravaginal ES is likely to have a larger effect."

Forty-four trials did not report the primary outcomes of perception of cure or improvement in OAB. The majority of trials were deemed to be at low or unclear risk of selection and attrition bias and unclear risk of performance and detection bias. Lack of clarity regarding the risk of bias was largely due to poor reporting. Many studies did not report whether electrical stimulation was safer than other treatments or if one type of electrical stimulation was safer than others.

Section Summary: Non-Neurogenic Urinary Dysfunction Including OAB
For individuals who have non-neurogenic urinary dysfunction including OAB who have failed behavioral and pharmacologic therapy and received an initial course of PTNS, a number of RCTs of PTNS have been published, including 2 key industry-sponsored RCTs, the OrBIT and SUmiT trials. Systematic reviews of the evidence have found short-term improvements with PTNS. The largest, highest quality study was the blinded sham-controlled SUmiT trial. This trial reported a statistically significant benefit of PTNS vs sham at 12 weeks. In an additional small sham-controlled trial, a 50% reduction in urge incontinent episodes was attained in 71% of the PTNS group compared with 0% in the sham group. The nonblinded OrBIT trial found that PTNS was noninferior to medication treatment at 12 weeks.

For individuals who have OAB syndrome who have failed behavioral and pharmacologic therapy and who respond to an initial course of PTNS and then receive maintenance PTNS therapy, there are up to 36 months of observational data available that suggest there is a durable effect for some of these patients. The SUmiT and OrBIT trials each included extension studies, which followed individuals who responded to the initial course of PTNS and continued to receive periodic maintenance therapy. There is variability in the interval between and frequency of maintenance treatments, and an optimal maintenance regimen remains

unclear. While comparative data are not available after the initial 12-week treatment period, the observational data support a clinically meaningful benefit for use in individuals who have already failed behavioral and pharmacologic therapy and who respond to the initial course of PTNS. PTNS may allow such individuals to avoid more invasive interventions. Adverse events appear to be limited to local irritation for both short and long-term PTNS use.

NEUROGENIC BLADDER DYSFUNCTION

Schneider et al (2015) published a systematic review of the literature on tibial nerve stimulation (transcutaneous and percutaneous) for treating neurogenic lower urinary tract dysfunction. 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 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 (TTNS), 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 OAB (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 (e.g., maximum cystometric capacity, maximum detrusor pressure). In the articles reporting on RCT results, none reported statistically significant between-group differences in clinical outcome variables (e.g., number of episodes of urgency, frequency, nocturia).

Section Summary: Neurogenic Bladder Dysfunction

Few RCTs evaluating tibial nerve stimulation for treating neurogenic bladder have been published to date, and all but one 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 cleared by the U.S. FDA for the treatment of fecal incontinence. 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, Edenfield et al (2015) identified 17 studies consisting of 13 case series and 4 RCTs. Three of the RCTs evaluated transcutaneous electrical nerve stimulation, and one used PTNS. A systematic review by Horrocks et al (2014) identified the same RCT, George et al (2013; detailed below); the review also identified an RCT comparing PTNS with TTNS. Horrocks identified 5 case series and an 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 et al (2014) analysis lacked a control group.

Two sham-controlled randomized trials and an RCT comparing PTNS with sacral nerve stimulation (SNS) have been identified. The first sham-controlled trial was published by George et al (2013) 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 endpoint 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 trial, and data were analyzed on an intention-to-treat 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 endpoint; the difference among groups was not statistically significant (p=0.035). All 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 randomized trial, known as CONFIDeNT, was published by Knowles et al (2015) in the U.K. The trial 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 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 two-week bowel diaries. Twelve patients withdrew from the trial. 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 the 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 compared with 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).

Thin et al (2015) published data on PTNS vs SNS for fecal incontinence. 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 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: 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 randomized trial 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 the superiority of PTNS over sham treatment. Systematic reviews have not conducted pooled analyses.

SUMMARY OF EVIDENCE
For individuals who have non-neurogenic urinary dysfunction including OAB who have failed behavioral and pharmacologic therapy who receive an initial course of PTNS, the evidence includes randomized sham-controlled trials, RCTs with an active comparator, and systematic reviews. Relevant outcomes are symptoms, change in disease status, functional outcomes, quality of life, and treatment-related morbidity. The SUmiT and the OrBIT trials are 2 key industry-sponsored RCTs. Systematic reviews that include these trials and other published trials have found short-term improvements with PTNS. The largest, highest quality study was the double-blinded, sham-controlled SUmiT trial. It reported a statistically significant benefit of PTNS vs sham at 12 weeks. In an additional small sham-controlled trial, a 50% reduction in urge incontinent episodes was attained in 71% of PTNS group compared with 0% in the sham group. The nonblinded OrBIT trial found that PTNS was noninferior to medication treatment at 12 weeks. Adverse events were limited to local irritation effects. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

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

For individuals who have neurogenic bladder dysfunction who receive PTNS, the evidence 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

one performed transcutaneous stimulation rather than PTNS. Studies varied widely in factors, such as the study populations and comparison interventions. 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.

For individuals who have fecal incontinence who receive PTNS, the evidence 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 randomized trial did find a significantly greater decrease in the absolute number of weekly incontinence episodes in the active treatment group, but the overall trial findings did not suggest the 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.

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Policy History

Original Effective Date: 04/16/2014
Current Effective Date: 06/20/2018

04/06/2014	Medical Policy Committee review
04/16/2014	Medical Policy Implementation Committee approval. New policy.
07/10/2014	Medical Policy Committee review
07/16/2014	Medical Policy Implementation Committee approval. Coverage changed from investigational to eligible for coverage with criteria for selected patients with non-neurogenic overactive bladder. Posterior tibial nerve stimulation is investigational when Patient Selection Criteria are not met and in all other situations.
06/04/2015	Medical Policy Committee review
06/17/2015	Medical Policy Implementation Committee approval. No change to coverage.
08/03/2015	Coding update: ICD10 Diagnosis code section added; ICD9 Procedure code section removed.

Percutaneous Tibial Nerve Stimulation

Policy # 00415
Original Effective Date: 04/16/2014
Current Effective Date: 06/20/2018

06/02/2016	Medical Policy Committee review
06/20/2016	Medical Policy Implementation Committee approval. No change to coverage.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
09/07/2017	Medical Policy Committee review
09/20/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
06/07/2018	Medical Policy Committee review
06/20/2018	Medical Policy Implementation Committee approval. Title changed from "Posterior Tibial Nerve Stimulation for Voiding Dysfunction" to " Percutaneous Tibial Nerve Stimulation". Revised eligible for coverage statements for use of PTNS in OAB syndrome that has failed behavioral and pharmacologic therapy. In these patients, PTNS is considered eligible for coverage as an initial course of therapy and maintenance therapy for individuals who respond to initial course. Investigational statement edited to be investigational for all indications with bullet points for urinary and fecal incontinence. Added a Policy Guidelines section.

Next Scheduled Review Date: 06/2019

Coding

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Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	64566, 64999
HCPCS	No codes
ICD-10 Diagnosis	N32.81 N39.3 N39.41 N39.42 N39.43 N39.44 N39.45 N39.46 N39.490 N39.498 R32 R33.0 R33.8 R33.9 R35.0 R39.14 R39.15

Percutaneous Tibial Nerve Stimulation

Policy # 00415
Original Effective Date: 04/16/2014
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*****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. Food and Drug Administration (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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