Medical Policy

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Title: Tibial Nerve Stimulation

Related Policies	▪ *Injectable Bulking Agents for the Treatment of Urinary and Fecal Incontinence* ▪ *Sacral Nerve Neuromodulation / Stimulation*

Professional / Institutional
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Populations	Interventions	Comparators	Outcomes
Individuals: • With non-neurogenic urinary dysfunction including overactive bladder and have failed behavioral and pharmacologic therapy	Interventions of interest are: • Initial course of percutaneous tibial nerve stimulation	Comparators of interest are: • Sacral nerve stimulation • Botulinum toxin	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With overactive bladder syndrome who respond to an initial course of percutaneous tibial nerve stimulation	Interventions of interest are: • Maintenance percutaneous tibial nerve stimulation	Comparators of interest are: • Sacral nerve stimulation • Botulinum toxin	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With non-neurogenic urinary dysfunction including overactive bladder syndrome who have failed behavioral and pharmacologic therapy or responded to an initial course of percutaneous tibial nerve stimulation	Interventions of interest are: • Subcutaneous percutaneous tibial nerve stimulation	Comparators of interest are: • Sacral nerve stimulation • Botulinum toxin	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With neurogenic bladder dysfunction	Interventions of interest are: • Posterior tibial nerve stimulation	Comparators of interest are: • Conservative therapies • Medication • Sacral nerve stimulation • Botulinum toxin	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes • Quality of life • Treatment-related morbidity
Individuals: • With fecal incontinence	Interventions of interest are: • Posterior tibial nerve stimulation	Comparators of interest are: • Conservative therapies • Medication • Sacral nerve stimulation	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes • Quality of life

Populations	Interventions	Comparators	Outcomes
			• Treatment-related morbidity
Individuals: • With urge urinary incontinence and urinary urgency	Interventions of interest are: • Transcutaneous tibial nerve stimulation (eg, Vivally System)	Comparators of interest are: • Conservative therapies • Medication • Sacral nerve stimulation • Botulinum toxin	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes • Quality of life • Treatment-related morbidity

DESCRIPTION

Percutaneous tibial nerve stimulation (PTNS; also known as posterior tibial nerve stimulation) is an electrical neuromodulation technique used primarily for treating voiding dysfunction. Subcutaneous tibial nerve stimulation via an implantable peripheral neurostimulator is an alternate technique for treating urgency urinary incontinence associated with overactive bladder syndrome.

OBJECTIVE

The objective of this evidence review is to determine whether the use of percutaneous or subcutaneous tibial nerve stimulation improves the net health outcome in individuals who have urinary dysfunction associated with overactive bladder syndrome, neurogenic bladder, or fecal incontinence.

BACKGROUND

Voiding Dysfunction

Common causes of non-neurogenic voiding dysfunction are pelvic floor neuromuscular changes (eg, from pregnancy, childbirth, surgery), inflammation, medication (eg, diuretics, anticholinergics), obesity, and psychogenic factors. Overactive bladder is a non-neurogenic voiding dysfunction characterized by urinary frequency, urgency, urge incontinence, and nonobstructive retention.

Neurogenic bladder dysfunction is caused by neurologic damage in patients with multiple sclerosis, spinal cord injury, detrusor hyperreflexia, or diabetes with peripheral nerve involvement. The symptoms include overflow incontinence, frequency, urgency, urge incontinence, and retention.

Treatment

Approaches to the treatment of incontinence differentiate between urge incontinence and stress incontinence. Conservative behavioral management such as lifestyle modification (eg, dietary changes, weight reduction, fluid management, smoking cessation) along with pelvic floor exercises and bladder training are part of the initial treatment of overactive bladder symptoms

and both types of incontinence. Pharmacotherapy is another option, and different medications target different symptoms. Some individuals experience mixed incontinence.

If behavioral therapies and pharmacotherapy are unsuccessful, percutaneous tibial nerve stimulation (PTNS), sacral nerve stimulation, or botulinum toxin may be recommended.

Percutaneous Tibial Nerve Stimulation
The current indication cleared by the U.S. Food and Drug Administration (FDA) for PTNS is overactive bladder and associated symptoms of urinary frequency, urinary urgency, and urge incontinence.

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.

Administration of PTNS consists of inserting 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.

Percutaneous tibial nerve stimulation is less invasive than traditional sacral nerve neuromodulation , which has been successfully used to treat 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.

Percutaneous tibial nerve stimulation has also been proposed as a treatment for non-neurogenic and neurogenic bladder syndromes and fecal incontinence.

Subcutaneous Tibial Nerve Stimulation
The current indication approved by the FDA for subcutaneous tibial nerve stimulation (STNS) is urgency urinary incontinence in individuals who are intolerant or who have had an inadequate response to more conservative treatments or who have undergone a successful trial of PTNS. STNS is administered through a coin-sized leadless battery-powered implant (see Regulatory section). STNS offers a less invasive alternative to traditional sacral nerve neuromodulation and offers a convenient delivery system for automated treatments without the need for chronic outpatient PTNS treatment sessions.

Transcutaneous Tibial Nerve Stimulation
The current indication approved by the FDA for transcutaneous tibial nerve stimulation (TTNS) (Vivally System; see Regulatory section) is for the treatment of individuals with the bladder conditions of urge urinary incontinence and urinary urgency. The device consists of a stimulator

that is worn on the ankle and delivers electrical signals to the tibial nerve. This is typically an at-home treatment.

REGULATORY STATUS

In 2005, the Urgent® PC Neuromodulation System was the initial PTNS device cleared for marketing by the FDA through the 510(k) process to treat patients suffering from urinary urgency, urinary frequency, and urge incontinence. Additional PTNS devices have been cleared for marketing through the 510(k) process. They are listed in Table 1.

The devices are not FDA cleared for other indications, such as the treatment of fecal incontinence.

Wireless technology is evolving for the treatment of overactive bladder. In March 2022, the eCoin® Peripheral Neurostimulator System (Valencia Technologies Corporation) became the first subcutaneous tibial nerve stimulation implant approved by the FDA through the premarket authorization (PMA) process for individuals with urgency urinary incontinence (P200036; FDA Product Code: QPT).

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	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	Treatment of patients with overactive bladder and associated symptoms of urinary urgency, urinary frequency, and urge incontinence
ZIDA Wearable Neuromodulation System	Exodus Innovations	Mar 2021	K192731	Treatment of patients with an overactive bladder and associated symptoms of urinary urgency, urinary frequency, and urge incontinence
Vivally System Wearable, Non-Invasive Neuromodulation System and Mobile Application	Avation Medical, Inc.	Apr 2023	K220454	Treatment of patients with bladder conditions of urinary incontinence and urinary urgency.

FDA: U.S. Food and Drug Administration

POLICY

A. Percutaneous tibial nerve stimulation for an initial 12-week course may be considered **medically necessary** for individuals with non-neurogenic urinary dysfunction including overactive bladder syndrome who meet the following criteria:

   1. Failed behavioral therapy following an appropriate duration of 8 to 12 weeks without meeting treatment goals, **AND**

   2. Failed pharmacologic therapy following 4 to 8 weeks of treatment without meeting treatment goals.

B. Maintenance therapy using monthly percutaneous tibial nerve stimulation is considered **medically necessary** for individuals following a 12-week initial course of percutaneous tibial nerve stimulation that resulted in improved urinary dysfunction meeting treatment goals.

C. Percutaneous tibial nerve stimulation is considered **experimental / investigational** for all other indications, including, but not limited to the following:

   1. Neurogenic bladder dysfunction.

   2. Fecal incontinence.

D. Subcutaneous tibial nerve stimulation delivered by an implantable peripheral neurostimulator system (e.g., eCoin) is considered **experimental / investigational** for all indications, including individuals with non-neurogenic urinary dysfunction including overactive bladder.

E. Transcutaneous tibial nerve stimulation (e.g., Vivally System) is considered **experimental / investigational** for individuals with bladder conditions of urge urinary incontinence and urinary urgency.

POLICY GUIDELINES

A. Individuals may be considered to have failed behavioral therapies following an appropriate duration of 8 to 12 weeks without meeting treatment goals.
B. Individuals may be considered to have failed pharmacologic therapies following 4 to 8 weeks of treatment without meeting treatment goals.
C. Annual evaluation by a physician may be performed to ensure efficacy is continuing for maintenance percutaneous tibial nerve stimulation treatments.
D. Blue Cross and Blue Shield of Kansas expects healthcare professionals who perform percutaneous tibial nerve stimulation will be appropriately trained and/or credentialed to provide the proper testing and assessment of the individual's condition. It would be highly unlikely that this training is possessed by providers other than those with training and expertise in urology or urogynecology.

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

RATIONALE

This evidence review was created using searches of the PubMed database. The most recent literature update was performed through March 27, 2025.

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 1 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. Randomized controlled trials 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.

PERCUTANEOUS TIBIAL NERVE STIMULATION FOR NON-NEUROGENIC URINARY DYSFUNCTION INCLUDING OVERACTIVE BLADDER

Clinical Context and Therapy Purpose

The purpose of percutaneous tibial nerve stimulation (PTNS) in individuals who have non-neurogenic urinary dysfunction including overactive bladder (OAB) and have failed behavioral and pharmacologic therapy or those with OAB who have responded to an initial course of PTNS, is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant populations of interest are:

- Individuals who have non-neurogenic urinary dysfunction including OAB who have failed behavioral and pharmacologic therapy, and
- Individuals with OAB responsive to an initial course of PTNS.

Interventions
The therapy being considered is PTNS as an initial or maintenance therapy. During PTNS, a needle is inserted above the medial malleolus into the posterior tibial nerve followed by the application of low-voltage (10 mA, 1-10 Hz frequency) electrical stimulation. Noninvasive PTNS may be 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.

Comparators
The following therapies are currently being used to make decisions about non-neurogenic urinary dysfunction: botulinum toxin and sacral nerve stimulation (SNS).

Botulinum toxin is injected into the detrusor muscle. However, the toxin increases the risk of urinary retention and is not recommended for patients with a history of urinary retention or recurrent urinary tract infection (UTI).

Sacral nerve stimulation may be conducted in an outpatient clinical setting using temporary wire leads. Due to the incidence of lead migration, a 2-step process in a surgical setting is recommended. In the initial test phase, wire leads are inserted under the skin and if 50% improvement is reported, the patient may elect permanent implantation with a pacemaker-like stimulator. If the test phase is unsuccessful, the leads are then removed.

Outcomes
The general outcomes of interest are reductions in symptoms (eg, self-reported assessment of symptoms, decrease in the number of voids per day) and improved quality of life. Outcomes are measured following the 12-week treatment regimen.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:
- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews
Wang et al (2020) evaluated PTNS for patients with OAB in a systematic review and meta-analysis that included 28 studies (N=2461).[1,] The efficacy of PTNS was compared to baseline information before treatment or other treatments (not specified). Reviewers included several trials discussed in the sections below: the Overactive Bladder Innovative Therapy (OrBIT) trial (Peters et al [2009]), the Sham Effectiveness in Treatment of Overactive Bladder Symptoms (SUmiT) trial (Peters et al [2010]), and the Finazzi-Agro et al (2010), Vecchioli-Scaldazza et al (2013), and Preyer et al (2015) trials. Results demonstrated that PTNS reduced the daily

frequency of the following symptoms: voiding (mean difference [MD], −2.48; 95% confidence interval [CI, −3.19 to −1.76), nocturia (MD, −1.57; 95% CI, −2.16 to −0.99), urgency episodes (MD, −2.20; 95% CI, −3.77 to −0.62), and incontinence episodes (MD, −1.37; 95% CI, −1.71 to −1.02). Percutaneous tibial nerve stimulation also improved maximum cystometric capacity (MD, 63.76; 95% CI, 31.90 to 95.61) and compliance (MD, 7.62; 95% CI, 0.61 to 14.63). The pooled success rate was 68% (95% CI, 59% to 78%). The most common complication following PTNS was pain at the puncture site.

Xiong et al (2021) performed a systematic review with meta-analysis of 6 RCTs (N=291) evaluating the efficacy of tibial nerve stimulation (either PTNS or transcutaneous tibial nerve stimulation [TTNS]) versus anticholinergic medications for OAB.[2,] The SUmIT trial and trials by Vecchioli-Scaldazza et al (2013) and Preyer et al (2015) were among those included. There was a significant reduction in urge incontinence episodes with tibial nerve stimulation versus anticholinergic medications (MD, -1.11; 95% CI, -1.66 to -0.55). However, tibial nerve stimulation and anticholinergic medications had comparable effects on micturition, nocturia, urgency, and voided volume. Discontinuation due to adverse events was lower with tibial nerve stimulation than with anticholinergic medications (odds ratio [OR], 0.13; 95% CI, 0.03 to 0.51).

Two systematic reviews that did not include a quantitative analysis evaluated PTNS for nonobstructive urinary retention. Coolen et al (2020) evaluated 8 studies, 5 of which reported the efficacy of PTNS and 2 of transcutaneous electrical nerve stimulation (TENS).[3,] The objective success rate for PTNS (defined as a decrease of at least 50% in the frequency or volume of catheterization per 24 hr) was 25% to 41%. The subjective success rate (defined as the patient's request for continued chronic treatment with PTNS) ranged from 25% to 41%. A subjective success rate of 80% was reported in 1 study of women who received transvaginal TENS. Ho et al (2021) evaluated 16 studies, 5 of which reported on the efficacy of PTNS and 11 that of sacral neuromodulation (also referred to as SNM).[4,] The success rate for PTNS (defined as at least a 50% reduction in symptoms) ranged from 50% to 60%, while the success rates for SNM (which had variable definitions across trials) ranged between 42.5% and 100% (median, 79.2%) for the test stimulation phase and 65.5% to 100% (median, 89.1%) in the long term (median follow, 42 months).

Tutulo et al (2018) searched the literature through December 2017 and identified 21 studies using either SNS or PTNS to treat lower urinary tract dysfunction and chronic pelvic pain not responding to standard therapies.[5,] Reviewers concluded that both SNS and PTNS were effective therapies. Percutaneous tibial nerve stimulation demonstrated higher success rates (≥50% reduction in leakage episodes) and fewer side effects compared with SNS; however, longer follow-up studies with PTNS are needed. Another systematic review by Tutulo et al (2018) conducted a literature search through December 2017 of RCTs evaluating SNS and PTNS for the treatment of OAB unresponsive to standard medical therapy.[6,] Five RCTs were identified. Reviewers concluded that both SNS and PTNS, with success rates ranging from 61% to 90% and 54% to 79%, respectively, could be considered effective.

A Cochrane review by Stewart et al (2016) evaluated electrical stimulation with nonimplanted electrodes for OAB in adults.[7,] The literature search was current up to December 2015. The objective of the review was to determine whether electrical stimulation (including vaginal and rectal electrical stimulation, and PTNS) was better than no treatment or better than any other

treatment available for OAB. 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 (N=4424 randomized participants). Reviewers included several trials discussed below: the OrBIT (Peters et al [2009]) and OrBIT follow-up trials (MacDiarmid et al [2010]), the SUmiT trial (Peters et al [2010]), the Sustained Therapeutic Effects of Percutaneous Tibial Nerve Stimulation (STEP) trial (Peters et al [2013]), and the Finazzi-Agro et al (2010), Schreiner et al (2010), Vecchioli-Scaldazza et al (2013), and Preyer et al (2015) trials.

Data were obtained from the end of treatment and the longest available follow-up period. The primary outcomes identified were 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 events.

The key findings from the Cochrane review (2016) of evidence are summarized in Table 2. Percutaneous tibial nerve stimulation results were combined for vaginal and rectal electrical stimulation.

Table 2. Summary of Cochrane Systematic Review Outcomes

Comparators to Electrical Stimulation[a]	Electrical Stimulation Effect[a]	QOE
No active treatment, placebo, or sham		
Reduction in OAB symptoms	More effective	Moderate
Reduction in urge urinary incontinence	More effective	Moderate
Improvement in OAB-related quality of life	More effective	Moderate
Pelvic floor muscle training		
Reduction in OAB symptoms	More effective	Moderate
Reduction in urge urinary incontinence	Effect uncertain	No evidence
Improvement in OAB-related quality of life	Effect uncertain	Low
Drug therapy		
Reduction in OAB symptoms	More effective	Moderate
Reduction in urge urinary incontinence	Effect uncertain	No evidence
Improvement in OAB-related quality of life	Effect uncertain	No evidence
Oxybutynin or tolterodine		
Adverse events	Lower risk	Low
Placebo/sham		
Adverse events	Lower risk	Moderate

Adapted from Stewart et al (2016).[7,]
OAB: overactive bladder; QOE: quality of evidence.
[a]Electrical stimulation includes percutaneous tibial nerve stimulation.

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.

This review was informed by a TEC Assessment (2013) evaluating PTNS as a treatment for voiding dysfunction.[8,] It concluded that PTNS as a treatment for voiding dysfunction met TEC criteria and showed that PTNS improves the net health outcome. Specifically, PTNS ameliorated symptoms of chronic OAB or urinary voiding dysfunction, simultaneously improving quality of life parameters among patients who have failed behavioral and pharmacologic therapies.

In this assessment of 6 RCTs, TEC reviewers 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 about 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."

In 2012 and 2013, several other systematic reviews of the literature on PTNS for treating OAB were published.[9,10,11,12,] Only one conducted pooled analyses of study results.[9,] This review, by Burton et al (2012), conducted a pooled analysis of data from 4 trials (2 of which were abstracts) comparing PTNS with sham treatment. Reviewers found a significantly higher risk of successful treatment with PTNS (relative risk [RR], 7.02; 95% 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 below) contributed 220 (76%) of 289 patients in the pooled analysis.

Also, Shamliyan et al (2012) conducted a comparative effectiveness review for the Agency for Healthcare Research and Quality on the broader topic of nonsurgical treatments for urinary incontinence in adult women.[13,] Reviewers identified 4 RCTs comparing PTNS with no active treatment in patients with OAB. Two of the 4 RCTs reported 12-week results of the sham-controlled SUmiT trial; 1 of them included a subgroup of SUmiT participants and was only published as an abstract. The Shamliyan report included a pooled analysis of data from 3 studies that found a statistically significant 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 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).[14,] A limit of the Shamliyan et al (2012) analysis was that the 150

patients in the SUmiT subgroup analysis were included twice. The Shamliyan review did not discuss evidence on the efficacy of PTNS beyond 12 weeks.

Sham-Controlled Randomized Trials

The SUmiT trial, reported by Peters et al (2010), was a sham-controlled randomized trial.[15,] Before conducting the trial, investigators performed a pilot study in healthy volunteers to determine the adequacy of a sham PTNS intervention.[16,] The sham procedure was correctly identified by 10 (33%) of 30 volunteers. This percentage is below the 50% that could be expected by chance, so investigators concluded that the procedure was a feasible sham. Eligibility criteria included: a score of 4 or more on the Overactive Bladder Questionnaire Short Form (OAB-q SF) for urgency, self-reported bladder symptoms lasting at least 3 months, and having failed conservative care for these symptoms or a diagnosis of OAB. Overactive bladder 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 TENS surface electrodes were used. The TENS unit (Urgent PC system) delivered low-level stimulation to mimic 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 trial endpoint was an efficacy assessment measured by a 7-level global response assessment (GRA) tool, in which patients reported change in symptoms as markedly worse, moderately worse, mildly worse, the same, slightly improved, moderately improved, or markedly improved. A responder was defined as one who reported symptoms as moderately or markedly improved at week 13. The rate of responders was 54.5% (60/110) of PTNS subjects compared with 20.9% (23 of 110) of sham subjects. There was a statistically significant benefit reported with PTNS compared with sham treatment in voiding diary variables as well.

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 STEP trial, an extension of the SUmiT study, included only responders from the PTNS group.[17,] The purpose was to determine the threshold for maintenance therapy. Of the 60 PTNS group 13-week responders, 50 entered 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. Percutaneous tibial nerve stimulation was delivered when patients reported that their symptoms increased. Between 6 and 36 months, patients received a median of 1.1 monthly PTNS treatments 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 endpoint 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 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, UTI, 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) is a single-item subjective measure. An additional limitation was that only short-term comparative data were available. And 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.

Tables 3 and 4 summarize the SUmiT RCT and STEP extension studies.

Table 3. 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)[15,]; SUmiT	U.S.	23	2008-2009	110/103	110/105	GRA at 13 wk
Peters et al (2013)[17,]; 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 4. 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)[15,]				
GRA (13 wk)	60/110 (54.5)	23/110 (20.9)	NR	<.001
STEP (2013)[17,]				
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.

An RCT by Finazzi-Agro et al (2010) evaluated 35 women who had urge incontinence and detrusor overactivity on urodynamic testing.[14,] Patients were randomized 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 intention-to-treat. 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 Randomized Controlled Trials

An RCT comparing PTNS with medication for the treatment of OAB was published by Vecchioli-Scaldazza et al (2018).[18,] This 3-arm trial compared solifenacin (n=27), PTNS (n=34), and a combination of solifenacin plus PTNS (n=33) and followed patients through 10 months post treatment. Patients in all 3 arms experienced significant reductions from baseline in daytime frequency, night-time frequency, and urgency. Percutaneous tibial nerve stimulation was more effective than solifenacin alone, and the combination of PTNS plus solifenacin was more effective than PTNS alone. The combination therapy also showed the longest effect.

A group of RCTs has compared PTNS with an alternative treatment, medication, conservative therapy, or electrical stimulation.[14,19,20,21,22,23,18,] The trials reported inconsistent findings on short-term efficacy, and only 1 reported on the efficacy of PTNS beyond 12 weeks.

Three 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.[21,] There were no significant differences between groups on the reduction of incontinence episodes in 24 hours (p=.89) or quality of life (p=.07).

Another RCT comparing PTNS with solifenacin was a crossover trial published by Vecchioli-Scaldazza et al (2013).[22,] 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.

An RCT compared PTNS with conservative therapy. Schreiner et al (2010) assessed 51 women older than 60 years of age who complained of urge urinary incontinence.[23,] 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=.001).

Gungor Ugurlucan et al (2013) in Turkey compared transvaginal electrical stimulation (n=38) with PTNS (n=21) in women who had OAB.[20,] The electrical stimulation protocol consisted of 20-minute treatments, 3 times a week for 6 to 8 weeks. Percutaneous tibial nerve stimulation was performed with an Urgent PC device used for 12 weekly, 30-minute 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 in mean change in urgency episodes, nocturia, or incontinence episodes. 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=.54). 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=.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.

The OrBIT trial is the largest randomized trial that was not sham-controlled. This trial was a nonblinded comparison of PTNS and extended-release tolterodine (Detrol LA) in women with OAB.[24,] 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. 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. As expected, the mean reduction in voids of 1.8 for tolterodine and 3.6 for PTNS was based on previously published efficacy data. Study findings showed the noninferiority of PTNS based on results for 84 participants.

The trial also reported on secondary outcomes. There were no statistically significant differences between the PTNS and tolterodine groups for other symptoms recorded in the voiding diary. Improvement in all OAB symptom episodes was statistically significant within each group from baseline to 12 weeks, but not between groups.

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

MacDiarmid et al (2010) reported on 1-year follow-up data for patients from the OrBIT trial who had been assigned to the PTNS group and had reported symptom improvement at 12 weeks.[25,] Of the 35 responders, 33 were included. They received a mean of 12.1 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.

As noted, this analysis lacked data from the tolterodine group to assess 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 might have been subject to the placebo effect. Moreover, patients in the PTNS group who responded to initial treatment might have been particularly susceptible to a placebo response and/or might represent those with the best treatment response. Thus, these individuals

might also have been susceptible to a placebo response during maintenance treatments, especially treatments offered on an as-needed basis.

Tables 5 and 6 summarize the OrBIT and OrBIT 1-year follow-up studies.

Table 5. Summary of OrBIT RCT Characteristics

Study	Countries	Sites	Dates	Randomized/Completed		Outcome[a]
				PTNS	Tolterodine	
Peters et al (2009)[24,]	U.S.	11	2006-2008	50/41	50/43	Reported
MacDiarmid et al (2010)[25,] 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 6. Summary of OrBIT RCT Results

Study	Primary Outcome: Mean Reduction in Voids per Day (SD)			
OrBIT (2009)[24,]	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		<.001		<.001
Confidence interval		NR		NR
OrBIT 1-y follow-up (2010)[25,]	PTNS (n=25)			
	Baseline	12 Months		
Voids per day	12.4 (3.5)	-2.8 (3.7)	Not applicable	Not applicable
p		<.001		
Confidence interval		NR		

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

SECTION SUMMARY: PERCUTANEOUS TIBIAL NERVE STIMULATION FOR NON-NEUROGENIC URINARY DYSFUNCTION INCLUDING OVERACTIVE BLADDER

Initial Course of Percutaneous Tibial Nerve Stimulation

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 versus sham at 12 weeks. In another 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.

Maintenance Course of Percutaneous Tibial Nerve Stimulation

For individuals who have OAB syndrome who have failed behavioral and pharmacologic therapy, respond to an initial course of PTNS, and then receive maintenance PTNS therapy, there are up to 36 months of observational data 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 respond to the initial course of PTNS. Percutaneous tibial nerve stimulation 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. Typical regimens schedule maintenance treatments every 4 to 6 weeks.

SUBCUTANEOUS TIBIAL NERVE STIMULATION FOR NON-NEUROGENIC URINARY DYSFUNCTION INCLUDING OVERACTIVE BLADDER

Clinical Context and Therapy Purpose

The purpose of subcutaneous tibial nerve stimulation (STNS) in individuals who have non-neurogenic urinary dysfunction including overactive bladder (OAB) with episodes of urgency urinary incontinence and have failed behavioral and pharmacologic therapy or who have responded to an initial course of PTNS, is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant populations of interest are:

- Individuals who have non-neurogenic urinary dysfunction including OAB with episodes of urgency urinary incontinence who have failed behavioral and pharmacologic therapy, and
- Individuals with OAB with episodes of urgency urinary incontinence responsive to an initial course of PTNS.

Interventions

The therapy being considered is STNS. The eCoin Peripheral Neurostimulator System is an FDA-approved coin-sized leadless battery-powered implant that delivers electrical stimulation to the tibial nerve (0.5-15 mA, 20 Hz frequency). The recommended treatment duration is 30 minutes every 3 days for the first 18 weeks (42 sessions) and every 4 days thereafter and is programmed by the clinician. A patient controller can be leveraged to inhibit an automatic session in the event

of undesired or painful stimulation. The battery life is estimated at up to 3 years (range, 1-8 years).

Comparators
The following therapies are currently being used to make decisions about non-neurogenic urinary dysfunction: botulinum toxin and SNS.

Botulinum toxin is injected into the detrusor muscle. However, the toxin increases the risk of urinary retention and is not recommended for patients with a history of urinary retention or recurrent UTI.

Sacral nerve stimulation may be conducted in an outpatient clinical setting using temporary wire leads. Due to the incidence of lead migration, a 2-step process in a surgical setting is recommended. In the initial test phase, wire leads are inserted under the skin and if 50% improvement is reported, the patient may elect permanent implantation with a pacemaker-like stimulator. If the test phase is unsuccessful, the leads are then removed.

Outcomes
The general outcomes of interest are reductions in symptoms (eg, self-reported assessment of symptoms, decrease in the number of voids per day) and improved quality of life.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews
Amundsen et al (2024) conducted a systematic review and meta-analysis to indirectly compare the efficacy and safety of sacral neuromodulation (SNM) and implantable tibial neuromodulation (iTNM) for the treatment of OAB.[26,] Of the 20 studies included in the analysis, 3 were RCTs and the others were a prospective interventional, prospective observational, or retrospective studies. A total of 1766 patients treated with either SNM (n=1416) or iTNM (n=350) were included. The primary outcomes were the percentage of patients with a ≥ 50% reduction in urgency urinary incontinence (UUI) episodes, urinary frequency, and/or OAB symptoms. Primary safety measures included the rate of device-related adverse events. The primary results showed that the UUI responder rate was similar for both SNM and iTNM, with weighted averages of 71.8% and 71.3%, respectively. Similarly, weighted averages of OAB responder rates were 73.9% for SNM and 79.4% for iTNM. The rate of device-related AEs was 12.7% for SNM and 9.6% for iTNM. The authors concluded that both SNM and iTNM have similar efficacy and safety for the treatment of OAB and UUI, including significant improvements in quality of life and low rates of procedure and

device-related adverse events. Noted limitations included differences in study populations, geography, study methods, efficacy definitions, and stage of device development. Additionally, the length of follow-up data available for iTNM was shorter than for SNM, and none of the studies identified were direct comparisons of the two interventions.

Nonrandomized Studies

Rogers et al (2021) evaluated the safety and efficacy of the wireless eCoin device in a single-arm, open-label trial at 15 sites in the US.[27,] A total of 132 patients with refractory (failed ≥1 second or third-line therapy) OAB received the eCoin device and were included in the intention-to-treat analysis. The majority of patients were female (98%) and 26% had received prior PTNS therapy. At 24-week follow-up, 69% (CI, 61% to 77%) of patients had a 50% reduction in urge urinary incontinence symptoms based on 3-day voiding diaries and were considered "responders". Results were similar at weeks 36 and 48 with 70% (CI, 62% to 78%) and 68% (CI, 60% to 76%) of patients responding, respectively. Fewer patients reported 100% reduction in symptoms with only 21% of patients reporting 100% response at 48 weeks. By 48 weeks there was a mean decrease in urge urinary incontinence episodes (-2.61), urinary voids (-2.12), urgency episodes (-1.49), and nocturia episodes (-0.51). Outcomes were not stratified by prior treatments received. Outcomes were impacted by the COVID-19 pandemic. Pre-pandemic and in-person responder rates were 75% and 74%, respectively, whereas the responder rate during the pandemic was 60% (n=25) and the responder rate of remote visits was 57% (n=14). Adverse events related to the device or procedure were reported in 20% of patients and most were mild (11%) to moderate (6%). There were 3 severe adverse events, including 1 post-operative wound infection, 1 implant site infection, and 1 device stimulation issue. While the study met its primary performance goal of at least a 40% response rate after 48 weeks of therapy, the certainty of this data is limited by the lack of blinding and a control group and the fact that a performance goal was identified after patients had already been implanted.[28,] Thus, the FDA has required the manufacturer of the eCoin system to conduct a post-approval study to provide greater certainty of the potential benefit of the device. It is also intended to address safety concerns regarding device explantation and reimplantation following battery depletion given that the study observed the need to re-implant the device after only 1 year. Possible reasons for the negative impact of COVID-19 on the 48 week response rate were not explored.

A feasibility study conducted by MacDiarmid et al (2019) for the eCoin device conducted in the US and New Zealand initially enrolled 46 patients at 7 sites and found reduced urge urinary incontinence episodes at 3 months follow-up (from 4.2 to 1.7 daily episodes; p=.001).[29,] Subsequent long-term data published in 2021 indicate continued safety and efficacy of eCoin with 65% of patients considered responders and 26% of responders having complete continence at 12 months and only 1 serious infection-related adverse event.[30,] A follow-up study of 23 patients who were reimplanted with an eCoin device after 1 year with a second-generation device found reimplantation to be successful with 74% and 82% of patients having at least 50% reduction in episodes of urge urinary incontinence at 12 and 24 weeks, respectively.[31,] No serious device-related adverse events were reported.

Section Summary: Subcutaneous Tibial Nerve Stimulation for Non-Neurogenic Urinary Dysfunction Including Overactive Bladder

An open-label, single-arm study evaluating the first FDA-approved wireless subcutaneous tibial nerve stimulation device (eCoin) demonstrated a 68% response rate at 48 weeks of follow-up.

However, the certainty of the evidence is limited by the lack of comparator group and a lower response rate during the COVID-19 pandemic. An ongoing post-approval study may elucidate the certainty of benefit, including safety of reimplantation given battery lifespan concerns.

NEUROGENIC BLADDER DYSFUNCTION

Clinical Context and Therapy Purpose

The purpose of PTNS in individuals who have neurogenic bladder dysfunction is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations

The relevant population of interest is individuals with neurogenic bladder dysfunction. Symptoms may include urinating small amounts often, problems starting urination, problems emptying the bladder, inability to detect a full bladder, and losing bladder control.

Interventions

The therapy being considered is PTNS. During PTNS, a needle is inserted above the medial malleolus into the posterior tibial nerve followed by the application of low-voltage (10 mA, 1-10 Hz frequency) electrical stimulation. Noninvasive PTNS may be 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.

Comparators

The following therapies are currently being used to make decisions about neurogenic bladder dysfunction: conservative treatments (eg, medication to relax the bladder or to activate pelvic muscles, catheterization to empty the bladder, pelvic floor muscle training), botulinum toxin, and SNS.

Botulinum toxin is injected into the detrusor muscle. However, the toxin increases the risk of urinary retention and is not recommended for patients with a history of urinary retention or recurrent UTIs.

Sacral nerve stimulation may be conducted in an outpatient clinical setting using temporary wire leads. Due to the incidences of lead migration, a 2-step process in a surgical setting is recommended. In the initial test phase, wire leads are inserted under the skin and if 50% improvement is reported, the patient may elect permanent implantation with a pacemaker-like stimulator. If the test phase is unsuccessful, the leads are then removed.

Outcomes

The general outcomes of interest are reduced symptoms and improved quality of life. Outcomes are measured following the 12-week treatment regimen.

Study Selection Criteria

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews

Schneider et al (2015) published a systematic review on tibial nerve stimulation (transcutaneous and percutaneous) for treating neurogenic lower urinary tract dysfunction.[32,] In a literature search through January 2015, 16 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 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 (eg, maximum cystometric capacity, maximum detrusor pressure). None of the RCTs reported statistically significant between-group differences in clinical outcome variables (eg, number of episodes of urgency, frequency, nocturia).[33,34,35,36,]

Randomized Controlled Trials

Zonic-Imamovic et al (2019) published the results of an RCT evaluating treatment with oxybutynin compared to TTNS in multiple sclerosis patients with OAB.[37,] Patients were allocated to 2 groups of 30 patients each. Patients treated with anticholinergic therapy received 5 mg oxybutynin twice daily for 3 months. Patients treated with TTNS were treated at home daily for 30 minutes for 3 months. The OAB-q SF was utilized to assess the frequency of OAB symptoms and the quality of life of patients. For those treated with oxybutynin, the mean symptom subscale score improved from 61.9±6.0 to 32.4±14.8 ($p<.001$), and the mean quality of life subscale score improved from 27.8±13.7 to 56.1±17.3 ($p<.001$) after treatment. For those treated with TTNS, the mean symptom subscale score improved from 61.2±14.6 to 50.8±12.3 ($p=.004$) and the mean quality of life subscale score improved from 28.5±12.6 to 38.3±11.4 ($p=.003$). Final differences in symptoms and quality of life were found to be statistically significant between groups ($p<.001$) and favored treatment with oxybutynin.

A sham-controlled, double-blind RCT of TTNS in patients with neurogenic OAB and women with non-neurogenic OAB was conducted by Welk et al (2020) from January 2016 to March 2019.[38,] Fifty patients were recruited (OAB=20; neurogenic=30) and 24 were allocated to the sham group while 26 were allocated to active TTNS therapy. Baseline group characteristics were not specified but were noted to be similar. The majority of neurogenic OAB study participants had multiple sclerosis (22/30; 73%). The primary outcome measure was an improvement of patient perception of bladder condition (PPBC). Active responders did not significantly differ

between groups, numbering 3/24 (13%) in the sham group and 4/26 (15%) in the active group (p=.77). No significant differences in secondary outcome measures (24-hour pad weight, voiding diary parameters, condition-specific patient-reported outcomes) were noted. The end-of-study marginal mean PPBC score was 3.3 (95% CI, 2.8 to 3.7) versus 2.9 (95% CI, 2.5 to 3.4) in the sham versus active groups, respectively. Findings were not stratified according to neurogenic or non-neurogenic disease. The authors concluded that TTNS does not appear to be effective for treating symptoms in individuals with neurogenic or non-neurogenic OAB.

Sham-controlled trials of TTNS in individuals with acute spinal cord injury (TASCI; NCT03965299) and Parkinson disease (UROPARKTENS; NCT02190851) are ongoing.

Section Summary: 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 study populations and comparator interventions. Study findings have not suggested that tibial nerve stimulation significantly reduces incontinence symptoms and improves other outcomes.

FECAL INCONTINENCE

Clinical Context and Therapy Purpose
The purpose of PTNS in individuals who have fecal incontinence is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with fecal incontinence.

Interventions
The therapy being considered is PTNS. During PTNS, a needle is inserted above the medial malleolus into the posterior tibial nerve followed by the application of low-voltage (10 mA, 1-10 Hz frequency) electrical stimulation. Noninvasive PTNS may be 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.

Devices are not FDA cleared for the treatment of fecal incontinence.

Comparators
The following therapies are currently being used to make decisions about fecal incontinence: conservative therapies (eg, medical management, retraining of pelvic floor and abdominal wall musculature, dietary changes), medications, and SNS.

Sacral nerve stimulation may be conducted in an outpatient clinical setting using temporary wire leads. Due to the incidence of lead migration, a 2-step process in a surgical setting is recommended. In the initial test phase, wire leads are inserted under the skin, and if

improvement is reported after 2 weeks, the patient may elect permanent implantation with a pacemaker-like stimulator. If the test phase is unsuccessful, the leads are then removed.

Outcomes
The general outcomes of interest are reduced symptoms (eg, self-reported assessment of symptoms, a decrease in the number of voids per day) and improved quality of life. Outcomes are measured following the 6- to 12-week treatment regimen.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Systematic Reviews
Luo et al (2024) published a meta-analysis evaluating PTNS versus sham electrical stimulation for treatment of fecal incontinence in adults.[39,] The literature search was done through May 2022 and identified 4 RCTs (N=439). The analysis concluded that when compared to the control group, PTNS showed greater efficacy in lowering weekly episodes of fecal incontinence (MD, −1.6; 95% CI −2.94 to −0.26; p=.02; I^2=30%). A greater number of patients in the PTNS group also reported a weekly decrease in fecal incontinence episodes of more than 50% compared to the control group (RR, 0.73; 95% CI, 0.57 to 0.94; p=.02; I^2=6%). None of the fecal incontinence quality of life or St Mark's incontinence scores showed any significant differences between groups.

Sarveazad et al (2019) conducted a systematic review and meta-analysis investigating the role of tibial nerve stimulation versus sham in the control of fecal incontinence.[40,] A literature search conducted through December 2016 identified 5 studies including 249 patients treated with PTNS and 239 treated with sham. Studies utilizing transcutaneous stimulation were also eligible. A significant decrease in the number of fecal incontinence episodes was found in the PTNS group (standardized mean difference [SMD], -0.38; 95% CI, -0.67 to 0.10; I^2=32.8%; p=.009). However, no significant effect on incontinence scores (SMD, 0.13; 95% CI, -0.49 to 0.75; I^2=88.0%; p=.68), resting pressure (SMD, 0.12; 95% CI, -0.14 to 0.37; I^2=28.8%; p=.67), squeezing pressure (SMD, -0.27; 95% CI, -1.03 to 0.50; I^2=85.5%; p=.50), or maximum tolerable volume (SMD, -0.10; 95% CI, -0.40 to 0.20; I^2=0.0%; p=.52) was reported.

Tan et al (2019) published a systematic review and meta-analysis reporting placebo response rates in electrical nerve stimulation trials for fecal incontinence and constipation.[41,] A literature search was conducted through April 2017 identifying 10 randomized sham-controlled trials. Sham stimulation resulted in significant improvements in fecal incontinence episodes by 1.3 episodes per week (95% CI, -2.53 to -0.01; p=.05) and Cleveland Clinic Severity Scores by 2.2 points

(95% CI, 1.01 to 3.36; p=.0003). The authors note that these findings highlight the importance of sham controls in nerve stimulation trials.

Simillis et al (2018) conducted a systematic review and meta-analysis comparing PTNS with SNS for the treatment of fecal incontinence.[42,] The literature search identified 4 studies (1 RCT, 3 nonrandomized prospective studies) including 302 patients (109 undergoing SNS, 193 undergoing PTNS). The Cochrane Collaboration's risk of bias tool was used to assess study quality. Because none of the studies blinded participants and personnel, the risk of performance and detection biases were high. Attrition and publication biases were not detected. Meta-analysis showed that patients undergoing SNS experienced significant improvements compared with patients undergoing PTNS as measured on the Wexner Fecal Incontinence Score (weighted mean difference [WMD], 2.3; 95% CI, 1.1 to 3.4) and fecal incontinence episodes per week (WMD, 8.1; 95% CI, 4.1 to 12.1).

Edenfield et al (2015) conducted a literature search through November 2013 and identified 17 studies (4 RCTs, 13 case series) on the use of tibial nerve stimulation (percutaneous and transcutaneous) for the treatment of fecal incontinence.[43,] Three of the RCTs evaluated TENS and the other PTNS. The 1 RCT and 4 case series using PTNS reported significant decreases in weekly fecal incontinence episodes following 12 weeks of treatment. The quality of life domain scores (eg, depression, embarrassment, coping, lifestyle) showing significant improvements differed across the PTNS studies.

Horrocks et al (2014) conducted a literature search through February 2013 and identified 12 articles, 6 related to PTNS, 5 related to transcutaneous nerve stimulation, and 1 comparing both methods.[44,] One RCT, by George et al (2013),[45,] discussed below, was included in the Horrocks et al (2014) and the Edenfield et al (2015) reviews. Horrocks et al (2014) 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 PTNS treatment. In these studies, a median of 71% of patients (range, 63%-82%) reported at least a 50% reduction in episodes. The Horrocks (2014) analysis did not report on control groups.

Randomized Controlled Trials

George et al (2013) published the first sham-controlled trial.[45,] 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 differed 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 failed to 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 (p=.035). The mean number of incontinence episodes per week (standard deviation) at the end of the study was 1.8 (0.8), 5.1 (4.2), and 4.7 (3.5) in the PTNS, transcutaneous nerve stimulation, and sham groups, respectively (p=.04). These findings are limited by the small sample size and short-term follow-up.

A large sham-controlled randomized trial, known as CONFIDeNT, was by Knowles et al (2015).[46,] 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, 30-minute sessions. 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 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=.396). There was also no significant difference 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 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 6.9 and 4.8, respectively, in the sham group (MD, -2.26; 95% CI, -4.18 to -0.35; p=.021).

Horrocks et al (2017) conducted a post hoc analysis of data from the CONFIDeNT trial, to evaluate factors associated with the efficacy of PTNS for fecal incontinence.[47,] Results from the multivariable logistic regression on the outcome of 50% improvement in weekly fecal incontinence episodes found that age, fecal urgency, stool consistency, and severity of fecal incontinence did not affect response to PTNS. The presence of obstructive defecation was the only variable that negatively affected response to PTNS (OR, 0.4; 95% CI, 0.2 to 0.9). Excluding patients with obstructive defecation (n=112) resulted in a significant effect of PTNS compared with sham (49% vs 18%, p=.002).

Thin et al (2015) published data on PTNS versus SNS for fecal incontinence.[48,] Forty 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. Sacral nerve stimulation was provided using a 2-stage approach: a test stimulation was conducted first, 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. Rates at 3 months were 9 (47%) of 19 in the SNS group and 6 (38%) of 16 in the PTNS group. The authors did not conduct a direct statistical comparison of SNS and PTNS because the study was a pilot.

A single-center, investigator-blinded RCT compared PTNS (n=25) to anal inserts (n=25) in patients with fecal incontinence.[49,] At 3 months, a 50% reduction in weekly episodes of fecal incontinence, as calculated by a prospectively completed 2-week bowel diary, was found in 76% (19/25) of patients in the anal insert group and 48% (12/25) of patients in the PTNS group (p=.04). Both groups had similar improvements in St Mark's fecal incontinence scores and the International Consultation on Incontinence Questionnaire.

Zyczynski et al (2022) conducted the Neuromodulation for Accidental Bowel Leakage (NOTABLe) sham-controlled trial of PTNS in women with fecal incontinence (N=166).[50,] Women with greater than or equal to 3 months of moderate-to-severe fecal incontinence were randomized to PTNS (n=111) or sham stimulation (n=55). Stimulation was delivered in 12 weekly 30-minute sessions to a single lower extremity. The primary outcome was change from baseline in St. Mark score (a 7-item, validated patient-reported outcome) measured after 12 weekly treatments. Secondary outcomes included stool consistency, bowel movement, and stool leakage episodes per week. There was no significant difference between the PTNS group (-5.3 points) and the sham group (-3.9 points) in terms of improvement from baseline in St. Mark scores (adjusted difference -1.3; 95% CI, -2.8 to 0.2). There also was no significant difference in reduction in weekly fecal incontinence episodes from baseline between the PTNS group (-2.1 episodes) and sham group (-1.9 episodes) (adjusted difference -0.26; 95% CI, -1.85 to 1.33).

Nonrandomized Studies

Sanagapalli et al (2018) conducted a retrospective chart review of consecutive patients with multiple sclerosis-related fecal incontinence who had failed conservative therapy and who were subsequently treated with PTNS.[51,] Patients (N=33) received 8 weekly treatments of PTNS, with responders receiving an additional 4 weeks of treatment. Subjects were classified as responders based on the Wexner Fecal Incontinence Score if scores at the end of treatment were either half of the baseline score or if the score was less than 10. Twenty-six (79%) of the patients were classified as responders. Responders tended to be more symptomatic at baseline and had greater improvements in quality of life scores.

Section Summary: 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. None of the sham-controlled trials found that active stimulation was superior to sham for achieving a reduction in mean incontinence episodes. The sham-controlled randomized trial by Knowles et al found 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. The sham-controlled randomized trial by Zyczynski et al did not indicate a benefit of PTNS over sham stimulation either. A meta-analysis of 1 RCT and several observational studies reported that patients receiving SNS experienced significant benefits compared with patients receiving PTNS. A post hoc analysis of the larger trial suggested a subset of patients with fecal incontinence, those without concomitant obstructive defecation, might benefit from PTNS.

TRANSCUTANEOUS TIBIAL NERVE STIMULATION FOR URGE URINARY INCONTINENCE AND URINARY URGENCY

Clinical Context and Therapy Purpose

The purpose of transcutaneous tibial nerve stimulation in individuals with urge urinary incontinence and urinary urgency is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The following PICO was used to select literature to inform this review.

Populations
The relevant population of interest is individuals with bladder conditions of urge urinary incontinence and urinary urgency.

Interventions
The therapy being considered is transcutaneous tibial nerve stimulation. The device consists of a stimulator that is worn on the ankle and delivers electrical signals to the tibial nerve. This is typically an at-home treatment.

Comparators
The following therapies are currently being used to make decisions about bladder conditions of urge urinary incontinence and urinary urgency: conservative therapies (eg, medical management, pelvic floor muscle training, behavioral and dietary changes), medications, and SNS.

Outcomes
The general outcomes of interest are reduced symptoms (eg, self-reported assessment of symptoms, a decrease in the number of voids per day) and improved quality of life. Outcomes are measured following the 6- to 12-week treatment regimen.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

REVIEW OF EVIDENCE

Randomized Controlled Trials
Goudelocke et al (2025) conducted a multicenter, prospective, randomized, double-blind, sham-controlled trial to evaluate the effectiveness and safety of a home-based, transcutaneous tibial nerve stimulation system for the treatment of overactive bladder (OAB).[52,] The study included 125 adult subjects with OAB who were randomized 1:1 to receive either active therapy with the Vivally System or sham therapy. Patients were allowed to continue concomitant OAB medications if therapy was stable and they remained on a consistent regimen throughout the study. The primary efficacy endpoint was responder rate, defined as ≥50% reduction in daily urgency leaks or a ≥30% reduction in daily voids from baseline, recorded on an electronic voiding diary. A secondary analysis was done for individual symptoms. Safety was evaluated through adverse event reporting. Primary results showed that in the modified Intent-to-Treat (mITT) population (N=107), the responder rate was significantly higher in the active therapy arm compared to the sham arm (83.6% vs 57.7%; p=.032). A secondary analysis on individual symptoms showed no significant difference between the active therapy arm and the sham arm for voids (3.7 ± 4.4 vs 3.4 ± 6.0) or urgency leaks (2.6 ± 2.6 vs 3.1 ± 4.1). There were 20 device-related adverse events; thirteen of which (65.0%) were considered mild. The most common device-related

adverse event was pain or ache/cramping of the foot or ankle, which occurred in 8 patients. One out of 125 patients (0.8%) discontinued the study due to an adverse event determined to be unrelated to the system. No serious adverse events were reported. Trial characteristics and results are summarized in Tables 7 and 8. A limitation of the study is the primary efficacy endpoint was a composite of patient reported outcomes and the minimal clinically important difference was not specified. The statistical analysis was also not well described, lacking confidence intervals, p-values, and/or measures of variation for many of the outcome measure. Study relevance and study design and conduct limitations are summarized in Tables 9 and 10.

Table 7. Summary of Key RCT Characteristics

Study; Trial	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Goudelocke et al (2025)[52,]	US	8	NR	Individuals diagnosed with overactive bladder for at least 3 months	Transcutaneous tibial nerve stimulation (n=62)	Sham control (n=63)

NR: not reported.

Table 8. Summary of Key RCT Results

Study	Responder Rate, %	Voids, mean change from baseline	Urgency Leaks, mean change from baseline	Device-Related Adverse Events, n
Goudelocke et al (2025)[52,]	N=107	N=107	N=107	N=107
Transcutaneous tibial nerve stimulation (n=55)	83.6%	3.7 ± 4.4	2.6 ± 2.6	---
Sham control (n=52)	57.7%	3.4 ± 6.0	3.1 ± 4.1	---
Total (N=107)	---	---	---	20
p-value	.032	NR	NR	---

NR: not reported.

Table 9. Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Goudelocke et al (2025)[52,]				5. Clinically significant difference not specified 7. Primary efficacy endpoint was a composite score of patient reported outcomes	

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Population key: 1. Intended use population unclear; 2. Study population is unclear; 3. Study population not representative of intended use; 4, Enrolled populations do not reflect relevant diversity; 5. Other.
[b] Intervention key: 1. Not clearly defined; 2. Version used unclear; 3. Delivery not similar intensity as comparator; 4. Not the intervention of interest (e.g., proposed as an adjunct but not tested as such); 5: Other.
[c] Comparator key: 1. Not clearly defined; 2. Not standard or optimal; 3. Delivery not similar intensity as intervention; 4. Not delivered effectively; 5. Other.
[d] Outcomes key: 1. Key health outcomes not addressed; 2. Physiologic measures, not validated surrogates; 3. Incomplete reporting of harms; 4. Not establish and validated measurements; 5. Clinically significant difference not prespecified; 6. Clinically significant difference not supported; 7. Other.
[e] Follow-Up key: 1. Not sufficient duration for benefit; 2. Not sufficient duration for harms; 3. Other.

Table 10. Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Goudelocke et al (2025)[52,]					1. Power calculations not reported	3. Confidence intervals not reported for primary outcome and p-values not reported for secondary analysis 5. Incomplete description of statistical analysis; measures of variation not defined

The study limitations stated in this table are those notable in the current review; this is not a comprehensive gaps assessment.
[a] Allocation key: 1. Participants not randomly allocated; 2. Allocation not concealed; 3. Allocation concealment unclear; 4. Inadequate control for selection bias; 5. Other.
[b] Blinding key: 1. Participants or study staff not blinded; 2. Outcome assessors not blinded; 3. Outcome assessed by

treating physician; 4. Other.
[c] Selective Reporting key: 1. Not registered; 2. Evidence of selective reporting; 3. Evidence of selective publication; 4. Other.
[d] Data Completeness key: 1. High loss to follow-up or missing data; 2. Inadequate handling of missing data; 3. High number of crossovers; 4. Inadequate handling of crossovers; 5. Inappropriate exclusions; 6. Not intent to treat analysis (per protocol for noninferiority trials); 7. Other.
[e] Power key: 1. Power calculations not reported; 2. Power not calculated for primary outcome; 3. Power not based on clinically important difference; 4. Other.
[f] Statistical key: 1. Analysis is not appropriate for outcome type: (a) continuous; (b) binary; (c) time to event; 2. Analysis is not appropriate for multiple observations per patient; 3. Confidence intervals and/or p values not reported; 4. Comparative treatment effects not calculated; 5. Other.

Nonrandomized Studies

Goudelocke et al (2024) conducted a multicenter, open-label, single-arm study to evaluate the effectiveness and safety of a wearable transcutaneous tibial nerve stimulation system to treat OAB.[53,] The study included subjects with OAB (N=96), with a mean age of 60.8 ± 13.0 years, and 88.5% of the participants were female. The primary outcomes of interest were daily voids, incontinence, and urgency episodes, as well as quality of life (QOL) changes using The Overactive Bladder Quality of Life Questionnaire (OAB-q) and The Incontinence Quality of Life Questionnaire (I-QOL). The primary results showed significant reductions in 3-day diary parameters for daily voids (mean reduction of 2.84 ± 2.4; p<.0001), incontinence episodes (mean reduction of 1.91 ± 3.1; p<.0001), and urgency episodes (mean reduction of 3.09 ± 3.9; p<.0001) at 12 weeks. QOL improvements exceeded the minimal clinically important difference for all QOL questionnaires. There were 12 device-related adverse events, and no device-related serious adverse events. Mean therapy compliance at 12 weeks was 88.5%. Study characteristics and results are summarized in Tables 11 and 12. Some limitations include the open-label, single-arm study design, and subjects could either stay drug-naive or remain on a stable dose of concomitant OAB medications, confounding the effect of the device itself. Also, minimal clinically important differences were not reported for the primary outcomes. After the initial 12-week intervention there were 38 discontinuations or withdrawals from the study, so long-term follow-up data at 12 months was limited.

Table 11. Summary of Key Nonrandomized Trials Study Characteristics

Study	Study Type	Country	Dates	Participants	Treatment1	Follow-Up
Goudelocke et al (2024)[53,]	Open-label, single-arm	US	NR	Patients with overactive bladder	Transcutaneous tibial nerve stimulation	12 weeks

NR: not reported; US: United States.

Table 12. Summary of Key Nonrandomized Trials Study Results

Study	Daily Voids at 12 Weeks, mean reduction ± 95% CI	Incontinence Episodes at 12 Weeks, mean reduction ± 95% CI	Urgency Episodes at 12 Weeks, mean reduction ± 95% CI	Device-Related Adverse Events, n
Goudelocke et al (2024)[53,]	N=96	N=96	N=96	N=96
Transcutaneous tibial nerve stimulation	2.84 ± 2.4	1.91 ± 3.1	3.09 ± 3.9	12
p-value	<.0001	<.0001	<.0001	---

CI: confidence interval.

Section Summary: Transcutaneous Tibial Nerve Stimulation for Urge Urinary Incontinence and Urinary Urgency

One RCT and one nonrandomized study evaluating the treatment of urge urinary incontinence and urinary urgency using transcutaneous tibial nerve stimulation have been published to date. The results of the available studies did not show a clear benefit of transcutaneous tibial nerve stimulation. The RCT by Goudelocke et al (2025) showed statistically significant improvements in primary outcome measure. However, the primary outcome were a composite score of patient reported outcomes. A secondary analysis on individual symptoms showed no significant difference between the active therapy arm and the sham arm for voids or urgency leaks. The nonrandomized study by Goudelocke et al (2024) showed statistically significant improvements in daily voids, incontinence episodes, and urgency episodes. However, minimal clinically important differences were not reported for these outcomes.

SUPPLEMENTAL INFORMATION

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input 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.

2018 Input

Clinical input was sought to help determine whether the use of maintenance percutaneous tibial nerve stimulation (PTNS) for individuals with non-neurogenic urinary dysfunction including overactive bladder who have failed behavioral and pharmacologic therapy and respond to an initial course of PTNS would provide a clinically meaningful improvement in the net health outcome and whether the use is consistent with generally accepted medical practice. In response to requests, clinical input was received from 3 physician respondents identified by specialty societies.

For individuals with non-neurogenic urinary dysfunction including overactive bladder who have failed behavioral and pharmacologic therapy and respond to an initial course of PTNS, clinical input supports this use provides a clinically meaningful improvement in net health outcome and indicates this use is consistent with generally accepted medical practice.

Further details from clinical input are included in the Appendix.

Practice Guidelines and Position Statements
Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

American Urological Association et al
In 2019, the American Urological Association (AUA) and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) published updated guidelines on the diagnosis and treatment of non-neurogenic overactive bladder in adults.[54,] The guidelines included a statement that clinicians may offer PTNS as a third-line treatment option in carefully selected patients. The statement carried a grade C rating, indicating that the balance of benefits and risks/burdens are uncertain. In 2024, the AUA/SUFU published a guideline on the diagnosis and treatment of idiopathic overactive bladder.[55,] In the unabridged version of the guideline, PTNS is mentioned as a minimally invasive therapy option. The guideline states that "Clinicians may offer minimally invasive procedures to patients who are unable or unwilling to undergo behavioral, non-invasive, or pharmacologic therapies (Clinical Principle)" and " Clinicians may offer patients with OAB, in the context of shared decision making, minimally invasive therapies without requiring trials of behavioral, non-invasive, or pharmacologic management (Expert Opinion)". Transcutaneous tibial nerve stimulation is included in the list of non-invasive therapies in these guidelines.

American College of Obstetricians and Gynecologists
In 2015, the American College of Obstetricians and Gynecologists practice bulletin on the treatment of urinary incontinence in women did not address PTNS or other types of nerve stimulation.[56,]

American Gastroenterological Association
In 2017, the American Gastroenterological Association issued an expert review and clinical practice update on surgical interventions and device-aided therapy for the treatment of fecal incontinence.[57,] The update stated that "until further evidence is available, percutaneous tibial nerve stimulation should not be used for managing FI [fecal incontinence] in clinical practice."

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

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 13.

Table 13. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT05977634	The Efficacy of Transcutaneous Tibial Nerve Stimulation on Symptoms of Overactive Bladder and Quality of Life in Women With Idiopathic Overactive Bladder	26	Aug 2026
NCT05685433[a]	A Real World Study of eCoin for Urgency Urinary Incontinence: Post Approval Evaluation (RECIPE)	200	Dec 2030
NCT05882318[a]	Evaluating Effectiveness of Sensory and Subsensory Stimulation Amplitudes With eCoin® Tibial Nerve Stimulation in Urgency Urinary InContinence Episodes and Quality of Life (ESSENCE)	50	Jul 2024
NCT05422625	PTNS for Female Patients Suffering From Multiple Sclerosis (PTNS-MS)	34	Oct 2023
Unpublished			
NCT02190851	Evaluation of Treatment by Transcutaneous Electrical Nerve Stimulation (TENS) of the Posterior Tibial Nerve for Lower Urinary Tract Disorders in Parkinson's Syndrome (UROPARKTENS)	220	Oct 2020 (completed)
Terminated			
NCT05381116[a]	A Prospective, Sham-Controlled, Safety and Efficacy Study of a Smart, Self-Adjusting, Surgery-Free, Wearable Bladder Modulation and Digital Health System With Objective Confirmation of Nerve Activation for Use in Home by Subjects With Overactive Bladder Syndrome	125 (actual)	Jul 2023 (terminated)

NCT: national clinical trial.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS	
64555	Percutaneous implantation of neurostimulator electrode array; peripheral nerve (excludes sacral nerve)
64566	Posterior tibial neurostimulation, percutaneous needle electrode, single treatment, includes programming
C1607	Neurostimulator, integrated (implantable), rechargeable with all implantable and external components including charging system
E0737	Transcutaneous tibial nerve stimulator, controlled by phone application
0587T	Percutaneous implantation or replacement of integrated single device neurostimulation system for bladder dysfunction including electrode array and receiver or pulse generator, including analysis, programming and imaging guidance when performed, posterior tibial nerve
0588T	Revision or removal of percutaneously placed integrated single device neurostimulation system for bladder dysfunction including electrode array and receiver or pulse generator, including analysis, programming, and imaging guidance when performed, posterior tibial nerve
0589T	Electronic analysis with simple programming of implanted integrated neurostimulation system for bladder dysfunction (e.g., electrode array and receiver), including contact group(s), amplitude, pulse width, frequency (Hz), on/off cycling, burst, dose lockout, patient-selectable parameters, responsive neurostimulation, detection algorithms, closed-loop parameters, and passive parameters, when performed by physician or other qualified health care professional, posterior tibial nerve, 1-3 parameters
0590T	Electronic analysis with complex programming of implanted integrated neurostimulation system for bladder dysfunction (e.g., electrode array and receiver), including contact group(s), amplitude, pulse width, frequency (Hz), on/off cycling, burst, dose lockout, patient-selectable parameters, responsive neurostimulation, detection algorithms, closed-loop parameters, and passive parameters, when performed by physician or other qualified health care professional, posterior tibial nerve, 4 or more parameters
0816T	Open insertion or replacement of integrated neurostimulation system for bladder dysfunction including electrode(s) (e.g., array or leadless), and pulse generator or

	receiver, including analysis, programming, and imaging guidance, when performed, posterior tibial nerve; subcutaneous
0818T	Revision or removal of integrated neurostimulation system for bladder dysfunction, including analysis, programming, and imaging, when performed, posterior tibial nerve; subcutaneous

REVISIONS	
10-06-2014	Policy added to the bcbsks.com web site.
03-31-2015	Updated Description section
	Updated Rationale section
	Updated References section
03-02-2016	Updated Description section
	In Policy section: ▪ In Item A 3, removed "unless contraindicated" due to redundancy.
	Updated Rationale section
	Updated References section
08-08-2018	Updated Description section
	In Policy section: ▪ In Item A, added "for an initial 12-week course" and "urinary dysfunction including" to read, "Posterior tibial nerve stimulation for an initial 12-week course may be considered medically necessary in patients with non-neurogenic urinary dysfunction including overactive bladder syndrome who meet the following criteria:" ▪ Removed previous Item A 1, "Had symptoms of overactive bladder syndrome for at least 3 months, AND" ▪ In new Item A 1, added "following an appropriate duration of 8 to 12 weeks without meeting treatment goals and removed "see Policy Guidelines" to read, "Failed behavioral therapy following an appropriate duration of 8 to 12 weeks without meeting treatment goals," ▪ In new Item A 2, added "pharmacologic" and "following 4 to 8 weeks of treatment without meeting treatment goals" and removed "e.g., oral anti-muscarinics and/or transdermal oxybutynin unless contraindicated" to read, "Failed pharmacologic therapy following 4 to 8 weeks of treatment without meeting treatment goals." ▪ Added new Item B, "Maintenance therapy using monthly posterior tibial nerve stimulation is considered medically necessary for individuals following a 12-week initial course of posterior tibial nerve stimulation that resulted in improved urinary dysfunction meeting treatment goals." ▪ In new Item C, added "for", "indications", "including, but not limited to, the following", and "1. Neurogenic bladder dysfunction. 2. Fecal incontinence" and removed "in" to read, "Posterior tibial nerve stimulation is considered experimental / investigational for all other indications, including, but not limited to, the following: 1. Neurogenic bladder dysfunction. 2. Fecal incontinence." ▪ In Policy Guidelines, removed previous Items 1, 2, and 3, and added new Items 1-3.
	Updated Rationale section
	In Coding section: ▪ Removed ICD-9 codes.
	Updated References section
10-01-2018	Updated Description section
	Updated Rationale section

REVISIONS	
	Updated References section
02-24-2021	Updated Description section
	Updated Rationale section
	In Coding section • Added CPT codes: 0587T, 0588T, 0589T, 0590T • Added ICD-10 codes: R15.0, R15.1, R15.2, R15.9
	Updated References Section
10-19-2021	Updated Rationale Section
	Updated Description Section
	Updated Reference Section
Published 1-24-2023 Effective 02-23-2023	Updated Title to " Percutaneous Tibial Nerve Stimulation"
	Updated Description Section
	Updated Policy Section ▪ In statement A, B and C changed word "posterior" to "percutaneous"
	Updated Policy Guideline Section ▪ In Policy Guidelines C and D Changed word "posterior" to "percutaneous"
	Updated Coding Section ▪ Removed: 0587T, 0588T, 0589T, 0590T
	Updated Reference Section
	Removed Appendix
Published 10-02-2023 Effective 11-01-2023	Updated Title ▪ Changed title to "Percutaneous and Subcutaneous Tibial Nerve Stimulation"
	Updated Description Section
	Updated Policy Section ▪ Added: "Subcutaneous tibial nerve stimulation delivered by an implantable peripheral neurostimulator system (e.g., eCoin) is considered experimental / investigational for all indications, including individuals with non-neurogenic urinary dysfunction including overactive bladder.
	Updated Rationale Section
	Updated Coding Section ▪ Added 64555, 0587T, 0588T, 0589T, and 0590T ▪ Removed ICD-10 Codes
	Updated References Section
01-01-2024	Updated Coding Section ▪ Updated Nomenclature for 0587T, 0588T, 0589T, and 0590T ▪ Added 0816T and 0818T (eff. 01-01-2024)
10-22-2024	Updated Description Section
	Updated Rationale Section
	Updated Coding Section ▪ Added E0737 (eff. 10-01-2024)
	Updated References Section
Posted 06-24-2025; Effective 07-24-2025	Updated Title Section ▪ Title changed from: "Percutaneous and Subcutaneous Tibial Nerve Stimulation" to "Tibial Nerve Stimulation"
	Updated Description Section
	Updated Policy Section ▪ Added Section E: Transcutaneous tibial nerve stimulation (e.g., Vivally System) is considered experimental / investigational for individuals with bladder conditions of urge urinary incontinence and urinary urgency.

REVISIONS	
	Updated Rationale Section
	Updated Reference Section
01-01-2026	Updated Coding Section ▪ Added new code C1607 (eff. 01-01-2026)

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