Medical Policy

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***Current Policy Effective Date: 7/1/25**
(See policy history boxes for previous effective dates)

Title: Percutaneous Electrical Nerve Stimulation (PENS), Percutaneous Neuromodulation Therapy (PNT) and Restorative Neurostimulation Therapy

Description/Background

CHRONIC PAIN

A variety of chronic musculoskeletal or neuropathic pain conditions including low back pain, neck pain, diabetic neuropathy, chronic headache, and surface hyperalgesia, presents a substantial burden to patients. This pain and discomfort may, adversely affect one's ability to function and quality of life. Certain racial and ethnic groups are at a higher risk of developing diabetes, which may also put them at a greater risk of developing complications from diabetes, such as diabetic neuropathy. According to a 2018 to 2019 National Health Interview Survey and data from the Indian Health Service National Data Warehouse, American Indians and Alaska Natives had the highest reported rate of diagnosed diabetes at 14.5%.[1] This was followed by 12.1% of Black individuals, 11.8% of Hispanic individuals, 9.5% of Asian individuals, and 7.4% of White individuals having been diagnosed diabetes in 2018 or 2019 who may be impacted by chronic pain.

Treatment

These chronic pain conditions have typically failed other treatments such as rest, heat, or ice, over the counter pain relievers, physical therapy, and exercise techniques. Treatment modalities such as, percutaneous electrical nerve stimulation (PENS) percutaneous neuromodulation therapy (PNT) and restorative neuromodulation are being evaluated as alternatives to relieve chronic pain. Percutaneous electrical nerve stimulation (PENS), percutaneous neuromodulation therapy (PNT), and restorative neurostimulation therapy (ReActiv8) combine the features of electroacupuncture and transcutaneous electrical nerve stimulation. Percutaneous electrical nerve stimulation is performed with needle electrodes while PNT uses very fine needle-like electrode arrays placed near the painful area to stimulate peripheral sensory nerves in the soft tissue. ReActiv8 is an implantable electrical neurostimulation system that stimulates the nerves that innervate the lumbar multifidus muscles.

Percutaneous Electrical Nerve Stimulation
Percutaneous electrical nerve stimulation is similar in concept to transcutaneous electrical nerve stimulation (TENS) but differs in that needle's electrodes are inserted either around or immediately adjacent to the nerves serving the painful area and are then stimulated. Percutaneous electrical nerve stimulation is generally reserved for patients who fail to get pain relief from TENS. Percutaneous electrical nerve stimulation is also distinguished from acupuncture with electrical stimulation. In electrical acupuncture, needles are also inserted just below the skin, but the placement of needles is based on specific theories regarding energy flow throughout the human body. In PENS, the location of stimulation is determined by proximity to the pain.

Percutaneous Neuromodulation Therapy
Percutaneous neuromodulation therapy (PNT) is a variant of PENS in which fine filament electrode arrays are placed near the area causing pain. Some use the terms PENS and PNT interchangeably. It is proposed that PNT inhibits pain transmission by creating an electrical field that hyperpolarizes C fibers, thus preventing action potential propagation along the pain pathway. It consists of electrical stimulation on a peripheral nerve by using a needle as an electrode to lessen the pain and restore neuromuscular and nervous system functions

Restorative Neurostimulation Therapy
Restorative neurostimulation therapy (i.e., ReActiv8) is an implantable programmed electrical device used to deliver low level stimulation that proposes to restore neuromuscular control between the brain and the spine in those who have chronic low back pain as a result due to multifidus muscle dysfunction. The therapy provides bilateral stimulation using two electrical leads positioned for targeted electrical stimulation of the L2 branch of the dorsal ramus as it crosses the L3 transverse process. The therapy is proposed to be used for those who fail conservative treatment, such as pain medication and physical therapy, and for those who are not candidates for spine surgery.

Low Back Pain has become one of the most important drivers increasing the global disease burden despite intensive research efforts to enhance our understanding of its true causes and management. Also, it is rare (<5%) to clearly identify the specific cause of low back pain. The majority of causes (-90%) for low back pain are classified as non-specific, and occasionally, the cause may be attributed to radicular syndromes (-5%). Recently, there has been a growing focus on spinal function, specifically looking at the intrinsic paraspinal musculature and the role of the lumbar multifidi muscles in the cause, progression, and outcomes of low back pain.[51]

Regulatory Status

In 2002, the Percutaneous Neuromodulation Therapy™ (Vertis Neuroscience) was cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process. The labeled indication is: "… for the symptomatic relief and management of chronic or intractable pain and/or as an adjunctive treatment in the management of post-surgical pain and post-trauma pain."

In 2006, the Deepwave® Percutaneous Neuromodulation Pain Therapy System (Biowave) was cleared for marketing by FDA through the 510(k) process. FDA determined that this device was substantially equivalent to the Vertis neuromodulation system and a Biowave neuromodulation therapy unit. The Deepwave® system includes a sterile single-use percutaneous electrode array that contains 1014 microneedles in a 1.5-inch diameter area. The needles are 736 μm (0.736 mm) in length; the patch is reported to feel like sandpaper or Velcro. FDA product code: NHI.

In 2020, the ReActiv8 (Mainstay Medical) was FDA approved through the Premarket Approval (PMA) process (PMA P190021) for individuals with intractable chronic low back pain associated with multifidus dysfunction for whom available low back pain treatments do not provide sufficient or durable symptom relief.[2,]

Medical Policy Statement

Percutaneous electrical nerve stimulation is considered **experimental/investigational** for chronic pain. There is insufficient evidence that this device has been shown to improve net health outcomes.

Percutaneous neuromodulation therapy is considered **experimental/investigational** for chronic pain. There is insufficient evidence that this device has been shown to improve net health outcomes.

Restorative neurostimulation therapy is considered **experimental/investigational** for chronic pain. There is insufficient evidence that this device has been shown to improve net health outcomes.

Inclusionary and Exclusionary Guidelines

N/A

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure.)*

Established codes:

N/A

Other codes (investigational, not medically necessary, etc.):

64999 97039

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

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. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

PERCUTANEOUS ELECTRICAL NERVE STIMULATION

Clinical Context and Therapy Purpose

The purpose of percutaneous electrical nerve stimulation (PENS) in individuals who have pain 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 chronic musculoskeletal or neuropathic pain conditions including low back pain, neck pain, diabetic neuropathy, chronic headache, and surface hyperalgesia.

Interventions

The therapy being considered is PENS.

Comparators

The following practice is currently being used: continued medical management of chronic musculoskeletal or neuropathic pain conditions.

Outcomes

Specific outcomes of interest for individuals with chronic pain are listed in Table 1. The potential beneficial outcomes of primary interest would be improvements in pain, functioning, and quality of life.

Table 1. Outcomes of Interest for Individuals with Chronic Pain

Outcomes	Details

Morbid events	Opioid addiction, adverse events
Health status measures	Pain relief, functional status
Medication use	Number of unsuccessful medication trials, amount of medications needed, dose of medication, dose frequency

The Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT) recommends that chronic pain trials should consider assessing outcomes representing 6 core domains: pain, physical functioning, emotional functioning, participant ratings of improvement and satisfaction with treatment, symptoms and adverse events, and participant disposition.[3] Table 2 summarizes provisional benchmarks for interpreting changes in chronic pain clinical trial outcome measures per IMMPACT.[4]

Table 2. Benchmarks for Interpreting Changes in Chronic Pain Outcome Measures

Outcome Domain and Measure	Type of Improvement	Change
Pain intensity 0 to 10 numeric rating scale	Minimally important Moderately important Substantial	10 to 20% decrease ≥30% decrease ≥50% decrease
Physical functioning Multidimensional Pain Inventory Interference Scale Brief Pain Inventory Interference Scale	Clinically important Minimally important	≥0.6 point decrease 1 point decrease
Emotional functioning Beck Depression Inventory Profile of Mood States Total Mood Disturbance Specific Subscales	Clinically important Clinically important Clinically important	≥5 point decrease ≥10 to 15 point decrease ≥2 to 12 point change
Global Rating of Improvement Patient Global Impression of Change	Minimally important Moderately important Substantial	Minimally improved Much improved Very much improved

Regarding optimal timing of outcome assessment, this varies with pain setting.[5] Per IMMPACT, recommended assessment timing includes at 3, 6, and 12 months in patients with chronic low back pain, 3 to 4 months after rash onset in postherpetic neuralgia, 3 and 6 months in patients with painful chemotherapy-induced peripheral neuropathy, and at various timepoints in the chronic post-surgical pain setting (ie, 24 to 48 hours after surgery; 3, 6, and 12 months; or surgery-specific times based on the natural history of acute to chronic pain transition).

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

Musculoskeletal Pain

Systematic Reviews

Plaza-Manzano et al (2020) evaluated the effects of PENS alone or as an adjunct to other interventions on pain and related disability in adults with musculoskeletal pain conditions.[6] This systematic review and meta-analysis included a total of 19 RCTs (Table 3). Overall, the results revealed poor quality of evidence (dependent upon the presence of study limitations, indirectness of evidence, unexplained heterogeneity or inconsistency of results, imprecision of results, and high probability of publication bias) suggesting that PENS alone is associated with a large effect compared with sham, and a moderate effect when compared with other interventions, for decreasing pain intensity in the short term. Additionally, the combination of PENS with other interventions had a similar poor quality of evidence for a moderate effect for reducing pain intensity than comparative intervention alone. No clear effects of PENS, either alone or in combination, on related disability were seen. None of the included trials were able to blind therapists. Ten of the trials rated a high risk of bias in the item of allocation concealment and 17 in the item of blinding of participants. Beyond these 2 items, the risk of bias in the included trials was low. Of note, the quality of included evidence was negatively impacted by the presence of heterogeneity in the data and an insufficient number of participants to meet the desired significance and power in some RCTs.

Beltran-Alacreu et al (2022) evaluated the effectiveness of PENS compared to transcutaneous electrical nerve stimulation (TENS) on the reduction of musculoskeletal pain.[7] This systematic review and meta-analysis included a total of 9 RCTs in the qualitative analysis, with 7 in the quantitative analysis (N=527; Table 3). Overall, there was low-quality evidence for increased pain intensity reduction with PENS over TENS, but the difference found was not deemed to be clinically significant. When only studies with low risk of bias were meta-analyzed, there was a moderate quality of evidence that there is no difference between TENS and PENS for pain intensity. Six out of the 9 studies presented high risk for the blinding of participants, and 7 out of 9 were high risk for blinding of personnel. Beyond these 2 items, the risk of bias in the included trials was either low or unclear. Protocols and parameters for the application of PENS and TENS were heterogenous across all trials. The characteristics and results of both systematic reviews are presented in Tables 4 and 5, respectively.

Table 3. Randomized Controlled Trials Included in the Systematic Review/Meta-Analysis

Study	Plaza-Manzano et al (2020)[6]	Beltran-Alacreu et al (2022)[7]
Ghoname et al (1999)[8]	●	●
Ghoname et al (1999)[9]	●	●
Hamza et al (1999)[10]	●	
Weiner et al (2003)[11]	●	
Topuz et al (2004)[12]	●	●
Yokoyama et al (2004)[13]	●	●
Weiner et al (2008)[14]	●	
Perez-Palomares et al (2010)[15]	●	
Weiner et al (2007)[16]	●	
Weiner et al (2013)[17]	●	

Da Graca Tarrago et al (2016)[18]	●	
Elbadawy et al (2017)[19]	●	
Dunning et al (2018)[20]	●	
Da Graca Tarrago et al (2019)[21]	●	
Leon-Hernandez et al (2016)[22]	●	
Sumen et al (2015)[23]	●	
Medeiros et al (2016)[24]	●	
Botelho et al (2018)[25]	●	
Dunning et al (2018)[26]	●	
Yoshimizu et al (2012)[27]		●
Ng et al (2003)[28]		●
Tsukayama et al (2002)[29]		●
Cheng et al (1987)[30]		●
Lehmann et al (1986)[31]		●

Table 4. Characteristics of the Systematic Review/Meta-Analysis

Study	Dates	Trials	Participants	N (Range)	Design	Duration
Plaza-Manzano et al (2020)[6]	1999-2019	19	Studies that included adults with musculoskeletal pain receiving any type of PENS intervention compared to an acceptable comparator (sham, placebo, control, or another active intervention)	1617 (24-242)	RCT	Intervention duration (sessions/week) varied significantly among the included trials
Beltran-Alacreu et al (2022)[7]	1986-2012	9	Studies that compared TENS vs PENS in adults with musculoskeletal pain	527 (20-131)	RCT	Intervention duration range, 2 weeks to 6 months; follow-up range, 1 week to 8 months

PENS: percutaneous electrical nerve stimulation; RCT: randomized controlled trial; TENS: transcutaneous electrical nerve stimulation .

Table 5. Results of the Systematic Review/Meta-Analysis

Study	Pain intensity (short-term)			Pain intensity (mid-term)	Related disability (short-term)	Related disability (mid-term)
Plaza-Manzano et al (2020)[5]	PENS alone vs sham	PENS alone vs other intervention	PENS + other intervention vs same intervention alone	PENS alone or in combination vs comparative group	PENS alone or in combination vs comparative group	PENS alone or in combination vs comparative group
N	616	371	730	988	738	568
SMD (95% CI)	-1.22 (-1.66 to -0.79)	-0.71 (-1.23 to -0.19)	-0.70 (-1.02 to -0.37)	-0.68 (-1.10 to -0.27)	-0.33 (-0.61 to -0.06)	-0.21 (-0.52 to 0.10)
I^2 (p)	82% (<.001)	80% (.008)	75% (<.001)	89% (.001)	69% (.02)	71% (.19)
	Pain intensity (post-treatment)		**Pain intensity (follow-up 1 to 8 weeks)**		**Overall pain intensity**	
Beltran-Alacreu et al (2022)[7]	PENS vs TENS	PENS vs TENS (Low risk of bias only)	PENS vs TENS	PENS vs TENS (Low risk of bias only)	PENS vs TENS	PENS vs TENS (Low risk of bias only)
N	405	55	122	8	527	63

MD (95% CI)	-1.21 (-1.92 to -0.5)	-0.82 (-1.77 to 0.13)	-0.57 (-1.06 to -0.08)	-0.80 (-2.60 to 1.0)	-1.0 (-1.55 to -0.45)	-0.81 (-1.6 to 0.02)
p-value	.0008	.09	.02	.38	.0004	.06
I2 (p)	80% (<.0001)	0% (.68)	0% (.72)	NA	76% (<.00001)	0% (.86)

CI: confidence interval; MD: mean difference; NA: not applicable; PENS: percutaneous electrical nerve stimulation; SMD: standardized mean difference; TENS: transcutaneous electrical nerve stimulation .

Subsection Summary: Musculoskeletal Pain

Two systematic reviews have not revealed consistent benefit from PENS in musculoskeletal pain disorders. One review (19 RCTs, N=1617) concluded that PENS could decrease pain intensity but not related disability, while the other (9 RCTs, N=527) found no significant differences between PENS and TENS in mitigation of pain. These conclusions are uncertain due to important methodological limitations in individual trials included in these reviews, such as high heterogeneity with regard to application methods. Further well-designed RCTs evaluating the effects of PENS alone or in combination with other interventions is needed, particularly with longer term follow-up.

Chronic Low Back Pain

Randomized Controlled Trials

Weiner et al (2008) reported on an RCT with 200 older adults, which was funded by the National Institutes of Health.[14] Subjects with chronic low back pain were randomized to PENS or sham-control treatment, with or without physical conditioning/aerobic exercise, twice a week for 6 weeks. Thus, the 4 treatment groups were PENS alone, sham PENS alone, PENS plus physical conditioning, or sham PENS plus physical conditioning. The sham-control condition consisted of 10 acupuncture needles in identical locations, depth, and duration (30 minutes) as the PENS needles, with a brief (5-minute) stimulation from 2 additional needles. Primary and secondary outcome measures were collected at baseline, 1 week, and 6 months after treatment by a research associate unaware of the treatment. There were no significant adverse events and no differences between the PENS and sham PENS groups in any outcome measure at 1-week or 6-month follow-up. All 4 groups reported reduced pain of a similar level (improvement ranging from 2.3 to 4.1 on the McGill Pain Questionnaire), reduced disability (range, 2.1 to 3.0, on the Roland-Morris Disability Questionnaire), and improved gait velocity (0.04 to 0.07 m/s) that was maintained for 6 months. Although trialists concluded that minimal electrical stimulation (5 minutes with 2 needles) was as effective as usual PENS (30 minutes of stimulation with 10 needles), the lack of benefit of this treatment over the sham control did not support use of PENS in patients with chronic low back pain.

An earlier study by Weiner et al (2003) focused on chronic low back pain in 34 community-dwelling older adults.[11] Patients were randomized to twice weekly PENS or sham PENS for 6 weeks. At 3-month follow-up, the treatment group reported a significant reduction in pain intensity and disability, while the control group did not. Yokoyama et al (2004) used an active control of TENS in a study with 53 patients.[13] They reported that patients randomized to PENS twice weekly for 8 weeks (n=18) had significantly decreased pain levels, physical impairment, and nonsteroidal anti-inflammatory drug use, which continued 1 month after treatment completion compared with a second group that received PENS for 4 weeks followed by TENS for 4 weeks (n=17) and a third group that received only TENS for 8 weeks (n=18). While PENS for 8 weeks seemed to demonstrate greater effectiveness in controlling pain for up to 1 month after treatment compared with the other treatment groups, the beneficial effects were not found at the 2-month follow-up.

Several studies were reported by a single academic research group. One of the reports by Ghoname et al (1999) compared sham PENS, active PENS, and TENS in 64 patients.[32] Active PENS achieved better outcomes than sham PENS on visual analog scale (VAS) pain scores and daily oral analgesic requirements and was better than sham PENS and TENS on physical activity, quality of sleep, and preference. Another report by Ghoname et al (1999) compared sham PENS, active PENS, TENS, and exercise therapy in 60 patients.[7] Active PENS resulted in better outcomes than all other modalities in terms of VAS pain, reduction in analgesic requirements, physical activity, quality of sleep, and preference. Hamza et al (1999) varied the duration of active electrical stimulation at 3 levels (15, 30, or 45 minutes) and compared them with sham stimulation in 75 patients.[9] These investigators confirmed that sham PENS had the least effect, and results were best when the stimulation lasted 30 or 45 minutes. Ghoname et al (1999) varied the frequency of the active electrical stimulus, also comparing it with sham stimulation, in 68 patients.[8] One level involved active stimulation with alternating 15-Hz and 30-Hz frequencies, while the other active levels had frequencies of 4 Hz and 100 Hz. The alternating frequency technique had the best results, superior to sham PENS.

Subsection Summary: Chronic Low Back Pain
The largest double-blinded, sham-controlled trial on PENS for chronic low back pain found no difference between the active (30 minutes with 10 needles) and sham PENS (5 minutes with 2 needles) at 1 week or 6 months after treatment. While other smaller studies have suggested that active PENS has effects that exceed placebo PENS in the short term, the trialists did not address long-term improvements in pain and functional outcomes, the objective of treating chronic low back pain. No studies on PENS for low back pain have been identified in the last decade.

Chronic Neck Pain

Randomized Controlled Trials
One study by White et al (2000) compared 2 locations of active stimulation with sham stimulation in 68 patients.[33] Local stimulation involved needle insertion at the neck, while remote stimulation entailed needles placed in the lower back. The sham condition received needles with no electrical stimulation at the neck. Outcomes were assessed immediately after completion of a 3-week treatment period. The local placement of active needles resulted in better pain relief, physical activity, quality of sleep, and analgesic use than the local sham treatment or remote active treatment. The study was described as investigator blinded. Withdrawals were not noted and no long-term outcome data was presented.

Subsection Summary: Chronic Neck Pain
This single study with short-term follow-up does not permit conclusions on the effectiveness of PENS for treating chronic neck pain.

Diabetic Neuropathy

Randomized Controlled Trials
In a crossover study by Hamza et al (2000) 50 patients with diabetic neuropathic pain for at least 6 months were randomized to receive either sham PENS or active PENS first in a 7-week study.[34] Racial and ethnic demographics of patients were not described. Outcomes were assessed 1 day after completion of a 3-week treatment period. Active PENS had better results

on VAS pain, activity, sleep, and analgesic use than sham PENS. The authors describe the study as investigator-blinded. No long-term outcome data were presented.

Subsection Summary: Diabetic Neuropathy
This single study does not permit conclusions on the effects of PENS for treating diabetic neuropathy.

Headache

Randomized Controlled Trials
Ahmed et al (2000) conducted a crossover study in 30 patients with longstanding headaches of 3 types: tension, migraine, and posttraumatic injury.[35] Two-week courses of active and sham PENS were compared. Outcomes were assessed at the completion of each treatment. Active PENS achieved better outcomes than sham PENS in terms of VAS pain, physical activity, and quality of sleep. Results did not vary by headache type. The investigators stated that the study was single-blinded but gave no details about blinding methods or whether withdrawals occurred. The report did not offer long-term outcomes data.

Subsection Summary: Headache
This single study does not establish the effectiveness of PENS for treatment of chronic headache.

Chronic Surface Hyperalgesia

Randomized Controlled Trials
Raphael et al (2011) reported on a multicenter double-blinded randomized crossover trial of a single PENS treatment compared with a sham treatment in 30 patients with surface hyperalgesia due to a variety of chronic pain conditions.[36] The pain diagnoses included surgical scar pain, occipital neuralgia, posttraumatic neuropathic pain, stump pain, inflammatory neuropathic pain, chronic low back pain, complex regional pain syndrome, pain following total knee arthroplasty (TKA), chronic cervical pain, and postherpetic neuralgia. The duration of pain ranged from 1 to 35 years (mean, 8.1 years). Subjective pain on a numeric rating scale (NRS) and a pressure pain threshold were measured before and 1 week after the single treatment, with a washout period of 4 weeks between treatments. Median NRS scores improved from 7.5 to 0.5 after active PENS and did not change after sham treatment (7.5 pre, 7.5 post). The mean pain pressure threshold improved from 202 to 626 grams after active PENS and did not change significantly after sham treatment (202 grams pre, 206 grams post). Blinding was maintained after the first treatment, but not after the second due to the tingling sensation with active PENS. Analysis of the first treatment showed a significant difference in NRS score change (3.9 vs 0.1) and in the pain pressure threshold (310 g vs 8 g) for the active compared with sham treatment.

Subsection Summary: Chronic Surface Hyperalgesia
A single study has reported positive effects on PENS for chronic surface hyperalgesia. Longer term follow-up in a larger sample is needed to evaluate the efficacy and confirm clinically meaningful durability of this treatment approach.

Section Summary: Percutaneous Electrical Nerve Stimulation
A systematic review concluded that PENS could decrease the level of pain intensity, but not related disability, in musculoskeletal pain disorders. However, the overall level of evidence was

low and there was heterogeneity with regard to application methods leading to the conclusion that there is still high uncertainty regarding the effectiveness of PENS for musculoskeletal pain. The highest quality trial on PENS for chronic low back pain found no difference between the active (30 minutes with 10 needles) and sham PENS (5 minutes with 2 needles) at 1 week or 6 months posttreatment. While other smaller studies have suggested that active PENS has effects that exceed sham in the short term, none addressed long-term reductions in pain and improvements in functional outcomes, the objective of treating chronic pain. Most of the studies on PENS were reported by a single academic research group (including Ghoname, Hamza, Ahmed, and White) over a decade ago. A more recent study has reported positive effects on PENS for chronic surface hyperalgesia at 1 week after treatment. Longer term follow-up in a larger sample of individuals is needed to evaluate the efficacy and confirm clinically meaningful durability of this treatment approach.

PERCUTANEOUS NEUROMODULATION THERAPY

Clinical Context and Therapy Purpose

The purpose of percutaneous neuromodulation therapy (PNT) in individuals who have pain 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 chronic musculoskeletal or neuropathic pain conditions including knee osteoarthritis.

Interventions

The therapy being considered is PNT.

Comparators

The following practice is currently being used: continued medical management of chronic musculoskeletal or neuropathic pain conditions.

Outcomes

Specific outcomes of interest for individuals with chronic pain are listed in Table 1. The potential beneficial outcomes of primary interest would be improvements in pain, functioning, and quality of life.

The IMMPACT recommends that chronic pain trials should consider assessing outcomes representing 6 core domains: pain, physical functioning, emotional functioning, participant ratings of improvement and satisfaction with treatment, symptoms and adverse events, and participant disposition.[2] Table 2 summarizes provisional benchmarks for interpreting changes in chronic pain clinical trial outcome measures per IMMPACT.[4]

Regarding optimal timing of outcome assessment, this varies with pain setting.[5] Per IMMPACT, recommended assessment timing includes at 3, 6, and 12 months in patients with chronic low back pain, 3 to 4 months after rash onset in postherpetic neuralgia, 3 and 6 months in patients with painful chemotherapy-induced peripheral neuropathy, and at various timepoints in the chronic post-surgical pain setting (ie, 24 to 48 hours after surgery; 3, 6, and

12 months; or surgery-specific times based on the natural history of acute to chronic pain transition).

Study Selection Criteria
See information under the first indication.

Review of Evidence

Knee Osteoarthritis
Kang et al (2007) reported a single-blinded trial that included 70 patients with knee osteoarthritis randomized to stimulation (at the highest tolerable intensity) or placement of electrodes (without stimulation).[37] Patients in the sham group were informed that they would not perceive the normal "pins and needles" with this new device. Patients received 1 treatment and were followed for 1 week. The neuromodulation group had 100% follow-up; 7 (20%) of 35 patients from the sham group dropped out. Visual analog scale pain scores improved immediately after active (from 5.4 to 3.2) but not sham (5.6 to 4.9) treatments. Visual analog scale scores did not differ significantly between the 2 groups at 48 hours posttreatment. Changes in the Western Ontario and McMaster Osteoarthritis Index scores were significantly better for stiffness (1-point change versus 0-point change) but not for pain or function at 48 hours.

Section Summary: Percutaneous Neuromodulation Therapy
One study was identified on PNT for osteoarthritis of the knee. Interpretation of this trial is limited by its lack of investigator blinding and 48-hour VAS pain scores, and a differential loss to follow-up in the 2 groups. These results raise questions about the effectiveness of the blinding, the contribution of short-term pain relief and placebo effects, and the duration of PNT treatment effects.

Restorative Neurostimulation Therapy

Clinical Context and Therapy Purpose

The purpose of restorative neurostimulation therapy in individuals with chronic pain conditions 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 chronic musculoskeletal or neuropathic pain conditions, including low back pain.

Interventions

The therapy being considered is restorative neurostimulation therapy. The ReActiv8 System is an implantable electrical neurostimulation system that stimulates
the nerves that innervate the lumbar multifidus muscles.

Comparators

The following practice is currently being used: continued medical management.

Outcomes

Specific outcomes of interest for individuals with chronic pain are listed in Table 1. The potential beneficial outcomes of primary interest would be improvements in pain, functioning, and quality of life.

The IMMPACT recommends that chronic pain trials should consider assessing outcomes representing 6 core domains: pain, physical functioning, emotional functioning, participant ratings of improvement and satisfaction with treatment, symptoms and adverse events, and participant disposition.[3] Table 2 summarizes provisional benchmarks for interpreting changes in chronic pain clinical trial outcome measures per IMMPACT.[4]
Regarding optimal timing of outcome assessment, this varies with pain setting.[5] Per IMMPACT, recommended assessment timing includes at 3, 6, and 12 months in individuals with chronic low back pain.

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 Trial

Restorative neurostimulation therapy with the ReActiv8 system has been evaluated in 1 multicenter, sham-controlled RCT enrolling 204 individuals with chronic, refractory low back pain (ReActiv8-B, NCT02577354). Study characteristics are summarized in Table 6. Control group participants received treatment with the ReActiv8 system set to deliver low-level stimulation. The primary endpoint was the difference in proportions of responders in the treatment and control groups. Response was defined as the composite of 30% or greater reduction in VAS and no increase in pain medications, assessed at 120 days. Following the 120-day randomized phase, participants in the control group were given the option to cross over to the intervention group and were followed along with the participants from the intervention group for up to 3 years. Primary study results were reported by Gilligan et al (2021).[38] Information on the RCT is also included in the FDA Summary of Safety and Effectiveness Data conducted as part of the premarket approval process.[39]

At 120 days, there was no difference between groups on the primary endpoint of treatment response (57.1% intervention vs 46.6% sham; p =.1377) or the individual components of the primary endpoint (see Table 7). The study investigators conducted prespecified secondary analyses of the primary outcome data, including the between-group difference in VAS at 120 days, a review of participants with increased pain medications, and a cumulative-proportion-of-responders analysis, which graphically displays the proportion of responders across the range of all possible cutoffs and is described as having greater statistical power than the comparison of proportions of the dichotomized primary outcome. The VAS mean change from baseline to 120 days favored the intervention group (-3.3 vs -2.4; p =.032), but it is unclear if the difference between groups (0.9 points) was clinically meaningful. The cumulative proportion-of-responders analysis similarly favored the intervention group (p =.0499). Nine participants in both the intervention and control groups had an increase in pain medication at 120 days, but the increase was unrelated to low back pain in 6 of 9 participants in the treatment group versus 0 of 9 in the control group.

Study limitations are summarized in Tables 8 and 9. Most importantly, the controlled phase was only 120 days. In the longer-term, uncontrolled follow-up phase of the trial, there was continued improvement in VAS scores over time in those who were assessed, but the lack of a control group and high attrition limits drawing conclusions from these results. Data was available for 176 of 204 participants at 1 year (86.3%),[38,] 156 of 204 participants (79%) at 2 years, [40,] and 130 of 204 (63.7%) at 3 years.[41,]

Cooley et al (2023) conducted a systematic review investigating the associations between morphologic changes of paraspinal muscles, specifically addressing multifidus muscles and its their relationship to low back pain and other related outcomes such as disability, radiculopathy, and physical workload. Reports indicate conflicting results. This study explored the lumbar multifidus muscle quality and the clinical outcomes relating to low back pain in 875 patients [487 females; mean (SD) age: 43.6 (10.2) years]. The MRI-based measurements of paraspinal muscle's cross-sectional area at L4 and L5 were investigated. In the multivariable analyses, muscle quality was significantly associated with disability (0–23 scale) [β: -0.74, 95% CI: -1.14, -0.34], leg pain intensity (0–10 scale) [β: -0.25, 95% CI: -0.46, -0.03], and current pain duration of more than 12 months [OR: 1.27, 95% CI: 1.03, 1.55]. Patients with higher lumbar multifidus muscle quality reported lower levels of low back pain-related disability and leg pain intensity, indicating that muscle quality may play a role in the etiology of lumbar spine disorders.[51] However, the clinical importance of these associations is uncertain due to the low magnitude of identified associations. More longitudinal studies are needed to understand the effect of lumbar multifidus muscle quality on lumbar-related pain and disability. The clinical importance of these findings is questionable, due to weak associations for all the outcomes. Additional studies into the potentially complex interactions between clinical measures, spinal pathology, and multifidus muscle quality should be performed to clarify the level of influence these three entities may have on each other, and how this might relate to clinical outcomes or guide the management of patients with lumbar-related pain.
Sayed et al (2022) examined painful lumbar spinal disorders as a leading cause of disability in the U.S. and worldwide. Although many established and emerging interventional procedures are currently available, there exists a need for a defined guideline for their appropriateness, safety, and effectiveness for treatment of pain and disability from lower back pain. The American Society of Pain and Neuroscience (ASPN) developed "Back Guidelines", a comprehensive review of interventional treatments for lower back disorders. The authors concluded that the ASPN Back Guideline represents the first comprehensive analysis and grading of the existing and emerging interventional treatments available for LBP. [52] These updated guidelines include the current standard of care (SOC) based on the available evidence within peer-reviewed literature. However, there were no specific recommendations for the utilization of "Restorative Neurostimulation / ReActiv8 neurostimulator" for lower back pain in the current ASPN Back Guidelines.

Schwab et al (2024) participated in the industry sponsored clinical trial RESTORE (NCT04803214) which is a post market multicenter, open label randomized controlled trial. Candidates were assessed for nonoperative chronic lower back pain (CLBP) associated with multifidus dysfunction, in persons who had no indication for or history of lumbar spine surgery. The trial included 25 sites in the United States and persons were recruited between July 2021 July 2023. A sample sized group of 203 people were chosen to participate in this study. Patients were randomized to two arms: control group with optimized medical management (OMM) or restorative neurostimulation using the ReActiv8 device.[53] The primary endpoint was improvement in the Oswestry Disability Index (ODI) at one year between the two arms and the secondary endpoints were improvements in the numeric rating scale (NRS) and the EuroQol Five Dimension score (EQ-5D-5L) in one year. Testing was statistically and clinically significant in the restorative neurostimulation arm compared to the OMM arm. However, participants in this trial were not blinded to their treatment, and as a result, those randomized to the control arm may have experienced a nocebo effect underestimating the clinical effect of OMM medical management. In addition, patients in the treatment arm may have experienced a placebo effect after being randomized to interventional treatment. Also, in the treatment arm, there were additional contact points that resulted in additional interventions that could have artificially inflated the healthcare utilization.

Table 6. Randomized Controlled Trial of Restorative Neurostimulation Therapy (ReActiv8) for Chronic Low Back Pain: Study Characteristics

Study	Countries	Sites	Dates	Participants	Interventions	
					Active	Comparator
Gilligan et al (2021)[38], NCT02577354	US, Australia	26	2016-2018	N = 204Age 22 to 75 years with nonneuropathic mechanical chronic LBP with pain on at least half of the days in the prior year, and continuing LBP despite 90 days of medical management; positive prone instability test suggesting impaired motor control of the multifidus muscle and consequent lumbar segmental instability	Restorative neurostimulation therapy with the ReActiv8 System programmed to a patient appropriate stimulation level	Active sham (ReActiv8 programmed to deliver low level stimulation)

LBP: low back pain

Table 7. Randomized Controlled Trial of Restorative Neurostimulation Therapy (ReActiv8) for Chronic Low Back Pain: Results

Study	Primary Outcome:Response (≥ 30% reduction in VAS and no increase	VAS Response at day 120 (component of primary endpoint)	Increase in pain medication at 120-day visit (component of primary endpoint)	Mean Change in VAS at day 120 (SD)

	in pain medications at day 120)			
Gilligan et al (2021)[38.] NCT02577354	204	102	201	201
ReActiv8	57.1%	58.8%	9 (6 unrelated to LBP)	-3.3 (2.7)
Sham Control	46.6%	48.6%	9 (0 unrelated to LBP)	-2.4 (2.9)
Difference (95% CI)	10.4% (-3.3% to 24.1%)			0.9
p-value	.1377	.1438	NA	.032

CI: confidence interval; LBP: low back pain; NA: not applicable; SD: standard deviation; VAS: visual analog scale.

Table 8. Randomized Controlled Trial of Restorative Neurostimulation Therapy (ReActiv8) for Chronic Low Back Pain: Study Relevance Limitations

Study	Population[a]	Intervention[b]	Comparator[c]	Outcomes[d]	Duration of Follow-up[e]
Gilligan et al (2021)[38.] NCT02577354	4. Race/ethnicity of participants not reported				1. Follow-up was 120 days in controlled phase

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 9. Randomized Controlled Trial of Restorative Neurostimulation Therapy (ReActiv8) for Chronic Low Back Pain: Study Design and Conduct Limitations

Study	Allocation[a]	Blinding[b]	Selective Reporting[c]	Data Completeness[d]	Power[e]	Statistical[f]
Gilligan et al (2021)[38.] NCT02577354						

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

Nonrandomized studies of restorative neurostimulation therapy for chronic low back pain are at high risk of bias due to lack of blinding, small sample sizes, high attrition, and no sham control, but are briefly discussed here for completeness. A prospective single-arm trial (ReActiv8-A; NCT01985230) was conducted at 9 sites in the United Kingdom, Belgium, and Australia to assess technical feasibility, performance, and safety of the ReActiv8 system. Participants were followed at 45, 90, 180, and 270 days, then annually for 4 years. Results at 1 year,[42] 2 years,[43] and 4 years[44] have been published. Of 53 participants enrolled, 33 completed 4-year follow-up. Of these, 73% had a clinically meaningful improvement of 2 points or greater on the low back pain Numeric Rating Scale and 76% had an improvement of 10 points or greater on the Oswestry Disability Scale.[44] A case series (N = 44) published in 2022 reported the experience of a single surgeon in Germany.[45] After 1 year of therapy, 68% of individuals with refractory chronic low back pain who received treatment with the Reactive8 device had moderate (30% or greater) reductions in pain and 52% had substantial (greater than 50%) reductions in pain.

A systematic review by Tieppo Francio et al (2023) indicated that chronic low back pain (CLBP) is multi-factorial in nature, with recent research highlighting the role of multifidus muscle dysfunction in a subset of non-specific CLBP.[54] These investigators developed a foundational reference that elucidated the pathophysiological cascade of multifidus dysfunction including how this group of lower back muscles contrasted with other common causes of CLBP and its effect response to restorative neuro-stimulation devices. This review included 194 articles. Multifidus dysfunction was diagnosed by a history of mechanical, axial, nociceptive CLBP and examination showing functional lumbar instability, which differs from other structural etiologies. Diagnostic images were used to grade multifidus atrophy and evaluate other structural pathologies. Restorative neuro-stimulation distinguishes itself from traditional neuro-stimulation in a way that treats a different etiology, targets a different anatomical site, and has a distinctive mechanism of action. The authors concluded that multifidus dysfunction has been proposed to result from loss of neuromuscular control that may manifest clinically as muscle inhibition leading to altered movement patterns. Restorative neuro-stimulation, a novel implantable neurostimulator system, stimulates the efferent lumbar medial branch nerve to elicit repetitive multifidus contractions. This intervention aims to interrupt the cycle of dysfunction, normalize multifidus activity incrementally, and potentially restore neuromuscular control. Assessment of the quality of the articles was not performed due to the heterogenicity of each of the 195 articles in the studies. Data synthesis and key summary of findings was presented in a descriptive format, rather than a quantitative format since this scoping review highlights a conceptual framework and does not compare the same intervention and outcomes within the same populations. More prospective studies with standardized protocols are needed to inform clinical practice.

Copley et al (2024) stated that CLBP is often associated with impaired motor control and degeneration of the lumbar multifidus muscles. Several studies have reported on the use of multifidus or medial branch stimulation of the multifidus muscle group as a treatment option.[55] In a systematic review and meta-analysis, these investigators examined the change in LBP intensity with multifidus stimulation. They carried out a comprehensive literature search from 2010 to 2022 for RCTs or prospective reports in adults with CLBP, treated for multifidus dysfunction with medial nerve stimulation via implanted or percutaneous device. Mean change (standard error) in pain intensity was extracted and data synthesized using a mixed effects regression with a random intercept for the study to account for repeated time-points. A total of 419 participants were enrolled in 6 studies; there were 25 effects (1 to 6 time-points per study), with follow-ups ranging from 1.5 to 48 months. The weighted pooled mean effect was a reduction in pain intensity (0 to 10 scale) of 2.9 units (95 % CI: 2.1 to 3.7). The 95 % prediction interval was a reduction in pain intensity of 0.6 to 5.2 units. The estimated probability of a reduction in pain of greater than 2 units in a new similar study was 0.84 (0.68 to 0.98). Meta-regression showed that a longer follow-up time was associated with greater reductions in pain

(0.25 units [0.16 to 0.34] per 6 months). The authors concluded that medial branch stimulation for the treatment of CLBP demonstrated a high probability of a clinically significant change in pain intensity; and longer duration of stimulation was associated with decreased LBP intensities. Key challenges regarding these trials, were a result of the studies not assessing functional capacity or patient-reported outcomes beyond 1 year.

Section Summary: Restorative Neurostimulation Therapy

The evidence includes 3 systematic reviews, 1 sham-controlled RCT (N = 204), 1 prospective single-arm trial (N = 53), and a case series (N = 44). Relevant outcomes are symptoms, functional outcomes, quality of life, and medication use. In the RCT, there was no difference between groups on the primary endpoint of treatment response at 120 days, defined as the composite of 30% or greater reduction in VAS and no increase in pain medications (57.1% intervention vs 46.6% sham; p =.1377). Prespecified secondary analyses of primary outcome data favored the intervention group, but clinical significance is unclear. An uncontrolled follow-up phase of the RCT reported continued improvement in pain scores over 3 years but results are at high risk of bias due to lack of a control group and high attrition. Nonrandomized studies are limited by lack of blinding, no sham control, high attrition and small sample sizes. Future longitudinal studies are needed to understand the effect of lumbar multifidus muscle quality on lumbar-related pain and disability.

SUMMARY OF EVIDENCE

For individuals who have chronic pain conditions (eg, back, neck, neuropathy, headache, hyperalgesia) who receive PENS, the evidence includes primarily small, controlled trials and 2 systematic reviews. Relevant outcomes are symptoms, functional outcomes, quality of life, and medication use. Two systematic reviews have not revealed consistent benefits from PENS in musculoskeletal pain disorders. One review concluded that PENS could decrease pain intensity but not related disability, while the other found no significant differences between PENS and TENS in mitigation of pain. These conclusions are uncertain due to important methodological limitations in individual trials included in these reviews, such as high heterogeneity with regard to application methods. In the highest quality trial of PENS conducted to date in chronic low back pain, no difference in outcomes was found between the active (30 minutes of stimulation with 10 needles) and the sham (5 minutes of stimulation with 2 needles) treatments. Smaller trials, which have reported positive results, are limited by unclear blinding and short-term follow-up. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have chronic pain conditions (eg, knee osteoarthritis) who receive PNT, the evidence consists of a RCT. Relevant outcomes are symptoms, functional outcomes, quality of life, and medication use. The single trial is limited by lack of investigator blinding, unclear participant blinding, and short-term follow-up. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have chronic pain conditions including low back pain who receive restorative neurostimulation therapy (ReActiv8), the evidence included 3 systematic reviews, 1 sham-controlled RCT (N = 204), 1 prospective single-arm trial (N = 53), and a case series (N = 44). Relevant outcomes are symptoms, functional outcomes, quality of life, and medication use. In the RCT, there was no difference between groups on the primary endpoint of treatment response at 120 days, defined as the composite of 30% or greater reduction in VAS and no increase in pain medications (57.1% intervention vs 46.6% sham; p =.1377). Prespecified secondary analyses of primary outcome data favored the intervention group, but clinical significance is unclear. An uncontrolled follow-up phase of the RCT reported continued improvement in pain scores through 3 years but results are at high risk of bias due to lack of a control group and high attrition. Nonrandomized studies are limited by lack of blinding, no sham control, high attrition and small sample sizes. Research indicates inconsistencies in the identification of the multifidus muscle as one of the major stabilizers for the lumbar spine. Additional evidence from longer-term randomized -controlled clinical trials is needed. Evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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.

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.

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (2013) published guidance on percutaneous electrical nerve stimulation (PENS).[55] It concluded that the "Current evidence on the safety of [PENS] for refractory neuropathic pain raises no major safety concerns and there is evidence of efficacy in the short term."

In September 2022, NICE published guidance on neurostimulation of lumbar muscles with the ReActiv8 system for refractory non-specific chronic low back pain. [56]
The guidance was based on a rapid review conducted in July 2021 and included the following statements:

- "Evidence on the efficacy and safety of neurostimulation of lumbar muscles for refractory non-specific chronic low back pain is limited in quantity and quality. Therefore, this procedure should only be used with special arrangements for clinical governance, consent, and audit or research."
- "Further research should include suitably powered randomised controlled trials comparing the procedure with current best practice with appropriate duration. It should report details of patient selection and long-term outcomes."

American Academy of Neurology et al

The American Academy of Neurology, American Association of Neuromuscular and Electrodiagnostic Medicine, and American Academy of Physical Medicine and Rehabilitation reaffirmed 2011 evidence-based guidelines on the treatment of painful diabetic neuropathy in 2016.[46] The guidelines concluded that, based on a class I study, electrical stimulation is probably effective in lessening the pain of painful diabetic neuropathy and improving quality of life and recommended that PENS be considered for the treatment of painful diabetic neuropathy (level B). The guidelines were retired and replaced in 2022 with a guideline dedicated to oral and topical treatment of painful diabetic polyneuropathy.[47] In these updated guidelines, there is no mention of any electrical stimulation strategies for pain.

American Society of Anesthesiologists et al

The 2010 Practice guidelines for chronic pain management from the American Society of Anesthesiologists and the American Society of Regional Anesthesia and Pain Medicine indicated that subcutaneous peripheral nerve stimulation may be used in the multimodal treatment of patients with painful peripheral nerve injuries who have not responded to other therapies (Category B2 evidence, observational studies).[50]

American College of Physicians and American Pain Society
Joint clinical practice guidelines on the diagnosis and treatment of low back pain from the American College of Physicians and the American Pain Society in 2007 indicated uncertainty over whether PENS should be considered a novel therapy or a form of electroacupuncture.[48] The guidelines concluded that PENS is not widely available. The guidelines also concluded that transcutaneous electrical nerve stimulation has not been proven effective for chronic low back pain. These guidelines were updated in 2017 and authors stated that evidence was insufficient to determine harms associated with PENS thus, no recommendation was made.[49]

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

Ongoing and Unpublished Clinical Trials
Some currently ongoing and unpublished trials that might influence this review are listed in Table 10.

Table 10. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT04803214[a]	ReActiv8 Stimulation Therapy vs Optimal Medical Management: A Randomized Evaluation	228	July 2025
NCT04243915	Effectiveness of Percutaneous Neuromuscular Electrical Stimulation on Lumbar Multifidus in Combination With a Protocol of Motor Control Exercises in Patients With Chronic Low Back Pain	64	Dec 2024
NCT04683042	Fibromyalgia TENS in Physical Therapy Study (TIPS): an Embedded Pragmatic Clinical Trial	450	Aug 2024

NCT: national clinical trial

Government Regulations
National/Local:

National Coverage Determination (NCD) for Assessing Patient's Suitability for Electrical Nerve Stimulation Therapy (160.7.1)
Effective date 6/19/2006

Indications and Limitations of Coverage
Electrical nerve stimulation is an accepted modality for assessing a patient's suitability for ongoing treatment with a transcutaneous or an implanted nerve stimulator.

Accordingly, program payment may be made for the following techniques when used to determine the potential therapeutic usefulness of an electrical nerve stimulator:

B. Percutaneous Electrical Nerve Stimulation (PENS)

This diagnostic procedure which involves stimulation of peripheral nerves by a needle electrode inserted through the skin is performed only in a physician's office, clinic, or hospital outpatient department. Therefore, it is covered only when performed by a physician or incident to physician's service. If pain is effectively controlled by percutaneous stimulation, implantation of electrodes is warranted.

As in the case of TENS (described in subsection A), generally the physician should be able to determine whether the patient is likely to derive a significant therapeutic benefit from continuing use of an implanted nerve stimulator within a trial period of 1 month. In a few cases, this determination may take longer to make. The medical necessity for such diagnostic services which are furnished beyond the first month must be documented.

NOTE: Electrical nerve stimulators do not prevent pain but only alleviate pain as it occurs. A patient can be taught how to employ the stimulator, and once this is done, can use it safely and effectively without direct physician supervision. Consequently, it is inappropriate for a patient to visit his/her physician, physical therapist, or an outpatient clinic on a continuing basis for treatment of pain with electrical nerve stimulation. Once it is determined that electrical nerve stimulation should be continued as therapy and the patient has been trained to use the stimulator, it is expected that a stimulator will be implanted, or the patient will employ the TENS on a continual basis in his/her home. Electrical nerve stimulation treatments furnished by a physician in his/her office, by a physical therapist or outpatient clinic are excluded from coverage by §1862(a)(1) of the Act. (See §160.7 for an explanation of coverage of the therapeutic use of implanted peripheral nerve stimulators under the prosthetic devices benefit.) See §160.27 for an explanation of coverage of the therapeutic use of TENS under the durable medical equipment benefit.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Cranial Electrotherapy Stimulation (CES) and Auricular Electrostimulation
- Interferential Stimulation (IFS) (Sympathetic Therapy)
- Microcurrent Electrical Neurostimulation (MENS) for Home Use (e.g., AlphaStim® PPM) (Retired)
- Sacral Nerve Neuromodulation/Stimulation
- Transcutaneous Electrical Modulation Pain Reprocessing (Scrambler Therapy)

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The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 3/18/25, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
12/19/03	12/19/03	1/21/04	Joint policy established
9/1/06	7/10/06	7/6/06	Routine maintenance
11/1/08	08/19/08	10/30/08	Routine maintenance
7/1/11	4/19/11	5/3/11	Routine maintenance
3/1/14	12/10/13	1/6/14	Routine maintenance. Policy updated to mirror BCBSA; added percutaneous electrical stimulation to policy. Title changed from "Percutaneous Neuromodulation Therapy" to "Percutaneous Electrical Nerve Stimulation (PENS) and Percutaneous Neuromodulation Therapy (PNT)."
1/1/16	10/13/15	10/27/15	Routine maintenance
1/1/17	10/11/16	10/11/16	Routine maintenance
11/1/17	8/15/17	8/15/17	Routine maintenance
11/1/18	8/21/18	8/21/18	Routine maintenance
11/1/19	8/20/19		Routine maintenance
11/1/20	8/18/20		Routine maintenance; 64999 added to policy
11/1/21	8/17/21		Routine maintenance
1/1/22	10/19/21		Routine maintenance Ref 1,2,3,4 (5-23) added
1/1/23	10/18/22		Routine maintenance (ls) Ref 6,39,42 added
1/1/24	10/17/23		Routine maintenance (jf) Vendor Managed: NA Added ref: 2,38,39,40,41,42,43,44,45 & 52 • Added Restorative Neurostimulation Therapy in the title and in description section Title change from Percutaneous Electrical Nerve Stimulation (PENS) and

			Percutaneous Neuromodulation Therapy (PNT) Title change to: Percutaneous Electrical Nerve Stimulation (PENS) and Percutaneous Neuromodulation Therapy (PNT), and Restorative Neurostimulation Therapy • Added ReActiv8 under regulatory section and in PICOS • Edit to the Medical Policy Statement added for chronic pain after E/I.
1/1/25	10/15/24		Routine maintenance (jf) Vendor Managed: NA
7/1/25	4/22/25		Routine maintenance (jf) Vendor Managed: NA Literature Review: Mainstay medical Reactive8 Ref Added: 51,52,53,54,55 MPS edited, updated E/I rationale and section summary Updated description of policy under treatment Post JUMP: • MPS was separated out according to the 3 devices percutaneous electrical nerve stimulation, percutaneous neuromodulation therapy and restorative neurostimulation. There was more description and information added to each device in the background section. • Title changed: removal of “and” Percutaneous Electrical Nerve Stimulation (PENS), Percutaneous Neuromodulation Therapy (PNT) and Restorative Neurostimulation Therapy

Next Review Date: 4th Qtr, 2026

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Not Covered.
BCNA (Medicare Advantage)	See the Governmental Regulations section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.