Title: Peripheral Subcutaneous Field Stimulation and Peripheral Nerve Stimulation

Description/Background

CHRONIC PAIN
Chronic, noncancer pain is responsible for a high burden of illness. Common types of chronic pain are lumbar and cervical back pain, chronic headaches, and abdominal pain. All of these conditions can be challenging to treat.

Treatment
Pharmacologic agents are typically the first-line treatment for chronic pain, and several classes of medications are available. They include analgesics (opioid and nonopioid), antidepressants, anticonvulsants, and muscle relaxants. A variety of nonpharmacologic treatments also exist, including physical therapy, exercise, cognitive-behavioral interventions, acupuncture, and chiropractic and therapeutic massage.

Neuromodulation, a form of nonpharmacologic therapy, is usually targeted toward patients with chronic pain refractory to other modalities. Some forms of neuromodulation, such as transcutaneous electrical nerve stimulation (TENS) and spinal cord stimulation, are established methods of chronic pain treatment. Peripheral nerve stimulation, which involves placement of an electrical stimulator on a peripheral nerve, is also used for neuropathic pain originating from peripheral nerves.

Peripheral Nerve Stimulation Therapy
Peripheral nerve stimulation (PNS), or percutaneous peripheral nerve stimulation, involves the implantation of electrodes near or on a peripheral nerve that is identified as transmitting pain to a specific area of the body. This is proposed for the treatment of chronic, refractory pain that is nonresponsive to conservative treatments. There is insufficient evidence to support the safety and effectiveness of PNS for the treatment of any indication including chronic pain.
Peripheral Subcutaneous Field Stimulation (Peripheral Nerve Field Stimulation-PNFS)
Peripheral subcutaneous field stimulation (PSFS) is a modification of peripheral nerve 
stimulation. In PSFS, leads are placed subcutaneously within the area of maximal pain. The 
objective of PSFS is to stimulate the region of affected nerves, cutaneous afferents, or the 
dermatomal distribution of the nerves, which then converge back on the spinal cord. Combined 
spinal cord stimulation plus PSFS is also being evaluated.

The mechanism of action in PNS and PSFS is unknown. Theories include an increase in 
endogenous endorphins and other opiate-like substances, modulation of smaller A delta and C 
fibers by stimulated large-diameter A beta fibers; local stimulation of nerve endings in the skin; 
local anti-inflammatory and membrane depolarizing effect; or a central action via antegrade 
activation of A beta nerve fibers. Complications of PNS/PSFS include lead migration or 
breakage and infection of the lead or neurostimulator.

Regulatory Status

StimRouter Neuromodulation System (Bioness Inc., Valencia, CA) received 510(k) approval in 
2015 as a class II device. The device is indicated for pain management in adults who have 
severe intractable chronic pain of peripheral nerve origin, as an adjunct to other modes of 
therapy (e.g., medication). It is not intended to treat pain in the craniofacial region.

StimQ Peripheral Nerve Stimulator (PNS) (Stimwave Technologies Incorporated, Ft. 
Lauderdale FL) system received 510(k) approval in 2017 as a class II device. The approval 
included indications for use: the device is indicated for pain management in adults who have 
severe intractable chronic pain of peripheral nerve origin, as the sole mitigating agent, or as an 
adjunct to other modes of therapy used in a multidisciplinary approach. The StimQ PNS 
System is not intended to treat pain in the craniofacial region. The StimQ Trial Lead Kit is only 
used in conjunction with the StimQ Stimulator Receiver Kit. The trial devices are solely used 
for trial stimulation (no longer than 30 days) to determine efficacy before recommendation for a 
permanent (long term) device.

In July 2018, the SPRINT® Peripheral Nerve Stimulation System (SPR Therapeutics, Inc) was 
cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) 
process (K181422). The FDA determined that this device was substantially equivalent to 
existing devices for use in pain management. Peripheral subcutaneous field stimulation is also 
an off-label use of spinal cord stimulation devices that have been approved by the FDA for the 
treatment of chronic pain.

Medical Policy Statement

Peripheral nerve stimulation (PNS) therapy and peripheral subcutaneous field stimulation 
(PSFS) is experimental/investigational. They have not been scientifically demonstrated to 
improve patient clinical outcomes.
Inclusionary and Exclusionary Guidelines (Clinically based guidelines that may support individual consideration and pre-authorization decisions)

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

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, two domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial 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.

Clinical Context and Therapy Purpose
The purpose of PNS therapy and PSFS in patients who have chronic neuropathic pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does PNS/PSFS improve the net health outcome in patients with chronic neuropathic pain?

The following PICO was used to select literature to inform this review.
**Populations**
The relevant population of interest is individuals with chronic neuropathic pain.

**Interventions**
The therapy being considered is PNS and PSFS.

PNS/PSFS is performed in inpatient and outpatient settings. Patients with chronic neuropathic pain are managed by general practitioners and, in cases that are difficult to treat, by pain specialists.

**Comparators**
The following therapies/tools/rules/practices are currently being used to make decisions about PNS/PSFS.

Comparators of interest are medication, exercise or physical therapy, and cognitive-behavioral therapy.

**Outcomes**
The general outcomes of interest are symptoms, functional outcomes, quality of life, and treatment-related morbidity.

As a chronic condition, a follow-up of at least 6 weeks to 12 months would be desirable to assess outcomes in chronic neuropathic pain.

**Review of Evidence**

**Randomized Controlled Trials**

In 2012, Silberstein et al. published a randomized, controlled, double-blinded multicenter study on the safety and efficacy of peripheral nerve stimulation (PNS) of the occipital nerves for the management of chronic migraine in 157 patients. The patients were randomized to active treatment (n=105) or sham treatment (n=52). The primary endpoint was a difference in the percentage of responders (defined as patients that achieved a ≥50% reduction in mean daily visual analog scale scores) in each group at 12 weeks. There was not a significant difference in the percentage of responders in the Active compared with the Control group (95% lower confidence bound (LCB) of -0.06; p = 0.55). However, there was a significant difference in the percentage of patients that achieved a 30% reduction (p = 0.01). Importantly, compared with sham-treated patients, there were also significant differences in reduction of number of headache days (Active Group = 6.1, baseline = 22.4; Control Group = 3.0, baseline = 20.1; p = 0.008), migraine-related disability (p = 0.001) and direct reports of pain relief(p = 0.001). The most common adverse event was persistent implant site pain. The authors concluded, although this study failed to meet its primary endpoint, this is the first large scale study of PNS of the occipital nerves in chronic migraine patients that showed significant reductions in pain, headache days, and migraine-related disability. Additional controlled studies are warranted in this highly disabled patient population with a large unmet medical need.

In 2016, Deer et al. published a prospective, multicenter, randomized, double-blinded, partial crossover study to assess the safety and efficacy of the StimRouter neuromodulation system in the treatment of 94 patients with chronic pain of peripheral nerve origin. After IRB approval,
patients were enrolled, implanted, and then followed for three months to assess efficacy and one year for safety based on Food and Drug Administration guidance. The patients were randomized to the treatment StimRouter group (45) or the control group (n=49). The primary efficacy endpoint, three months after randomization to treatment, demonstrated that patients receiving active stimulation achieved a statistically significantly higher response rate of 38% vs. the 10% rate found in the Control group (p = 0.0048). Improvement in pain was statistically significant between the randomized groups, with the treatment group achieving a mean pain reduction of 27.2% from Baseline to Month 3 compared to a 2.3% reduction in the Control group (p < 0.0001). During the partial crossover period, patients again demonstrated statistically significant improvement in pain relief with active stimulation compared to baseline. Further, the treatment group had significantly better improvement than the control group in secondary measures including but not limited to quality of life and satisfaction. Safety, assessed throughout the trial and with follow-up to one year, demonstrated no serious adverse events related to the device. All device-related adverse events were minor and self-limiting. However, the results need confirmation in additional randomized controlled trials (RCTs) with longer follow-up to draw conclusions. Studies should also compare StimRouter with other peripheral nerve stimulation systems such as spinal cord stimulation and alternative treatments.

Gilmore et al (2019) conducted a double-blinded, randomized, placebo-controlled study with twenty-eight lower extremity amputees with postamputation.3 The subjects underwent ultrasound-guided implantation of percutaneous PNS leads and were randomized to receive PNS (with SPRINT, SPR Therapeutics), or placebo for four weeks. The placebo group then crossed over and all subjects received PNS for four additional weeks. The primary efficacy endpoint evaluated the proportion of subjects reporting ≥50% pain reduction during one to four weeks. A greater proportion of subjects receiving PNS (n=7/12, 58%, p=0.037) demonstrated ≥50% reductions in average postamputation pain during weeks one through four compared with subjects receiving placebo (n=2/14, 14%). Two subjects were excluded from efficacy analysis due to eligibility changes. Greater proportions of PNS subjects also reported ≥50% reductions in pain (n=8/12, 67%, p=0.014) and pain interference (n=8/10, 80%, p=0.003) after 8 weeks of therapy compared with subjects receiving placebo (pain: n=2/14, 14%; pain interference: n=2/13, 15%). Limitations of the study included small number of subjects.

No sham- or active pain treatment-controlled randomized trials evaluating PSFS were identified. One crossover RCT compared levels of PSFS. McRoberts et al (2013) reported on a randomized, crossover trial of different types of PSFS in 44 patients with chronic back pain. In the first phase of the trial, patients rotated through 4 levels of PFS: minimal, subthreshold, low frequency, and standard stimulation.4 Of 30 patients who completed the first phase, 24 reported that pain was significantly reduced by at least 50% in all of the stimulation groups and were considered responders. In phase 2, a permanent PFSF system was placed in 23 responders. During the 52 weeks over which these patients were followed, reported mean visual analog scale scores, present pain index, and total scores on the Short-Form McGill Pain Questionnaire were significantly improved from baseline at all follow-up visits (p<0.001). Because this trial did not include a control group, the methodologic strength of these results is similar to that of an uncontrolled study.
Nonrandomized Comparative Study
In comparative study, Mironer et al (2011) used a 2-part evaluation of combined use of spinal cord stimulation and PSFS in patients with low back pain. In the first part of the study, 20 patients with failed back surgery syndrome or spinal stenosis underwent a trial with both spinal cord stimulation and PSFS and selected the type of stimulation they found most efficacious (program 1: spinal cord stimulation alone; program 2: peripheral subcutaneous field stimulation alone; program 3: combined spinal cord stimulation plus peripheral subcutaneous field stimulation). Patients were blinded to the differences among the programs (randomized order of presentation) and were encouraged to try each program for at least 8 hours; 79% of patients preferred the combined use of spinal cord stimulation plus PFSF. In the second part of the study, 20 patients were implanted with spinal cord stimulation and PSFS electrodes and selected which program they preferred (spinal cord stimulation and PSFS used simultaneously, spinal cord stimulation as anode and peripheral subcutaneous field stimulation as cathode, spinal cord stimulation as cathode and PSFS as anode). The programs were presented in a random order, and patients were blinded to the differences among the programs offered. Communication between spinal cord stimulation and PSFS was reported to provide wider coverage of axial pain, with an overall success rate (>50% pain relief) of 90%. The most effective program was spinal cord stimulation as cathode and PSFS as anode.

Case Series
Warner et al (2020) reports on a retrospective case series of adults undergoing PNS implantation from 2004 to 2017 at an academic medical center. The primary outcomes were changes in numeric rating scale (NRS) pain scores, opioid utilization in oral morphine milligram equivalent (MME), and self-reported patient functioning at 6 months postoperatively. Infectious and device-related complications were also assessed. A total of 72 patients underwent PNS implantation, including 59 patients that received a preceding PNS trial (59/78; 76% progression rate) and 13 that did not receive a PNS trial. The most common indication for stimulation was occipital neuralgia (47%) followed by lower-extremity neuropathies (17%). PNS implantation was associated with 6-month reductions in pain scores (7 [6, 8] baseline vs. 4 [2, 5] 6 months; P < 0.001) and opioid utilization (e.g., median 60 [31, 104] vs. 18 [0, 52] MME among those with baseline opioid use; P < 0.001). Median functional improvement was 73% (50%, 88%). Seven patients (10%) suffered a postoperative surgical site infection at a median of 50 (30, 124) days, of which five devices were removed. Although PNS was associated with reduced pain scores and lower opioid utilization, prospective multicenter evaluation is warranted to evaluate long-term outcomes.

In addition to the controlled studies, a number of case series have been published, several of which included 50 or more patients. Kloimstein et al (2014) reported on a prospective multicenter study of 118 patients treated with peripheral subcutaneous field stimulation for chronic low back pain. Before patients were implanted with the permanent PSFS system, trial stimulation was given for at least 7 days. The permanent stimulation system was implanted in 105 patients. Significant improvements occurred at the 1-, 3-, and 6-month post-implantation follow-ups in average visual analog score pain, Oswestry Disability Questionnaire, Beck Depression Inventory, and 12-Item Short-Form Health Survey scores. Significant reductions in use of opioids, nonsteroidal anti-inflammatory, and anticonvulsant medications were also reported.
Sator-Katzenschlager et al (2010) reported on a retrospective multicenter study of PSFS.⁸ A total of 111 patients with chronic focal noncancer pain were treated, including 29 patients with low back pain, 37 with failed back surgery syndrome, 15 with cervical neck pain, and 12 patients with postherpetic neuralgia. The median duration of chronic pain was 13 years, and the median number of previous surgeries was 2.7. For permanent implantation of the leads, patients had to have achieved at least 50% reduction in pain on a numeric rating scale during the trial period. After permanent implantation, pain intensity decreased in 102 (92%) patients. Mean pain intensity decreased from 8.2 at baseline to 4.0 at follow-up, with a concomitant reduction in consumption for analgesics and antidepressants. Lead dislocation or fracture occurred in 20 (18%) patients.

Verrills et al (2011) reported on a series of 100 patients treated with PSFS for chronic neuropathic pain. Indications included chronic pain occurring among varying regions: occipital/craniofacial (n = 40), lumbosacral (n = 44), thoracic (n = 8), groin/pelvis (n = 5), or abdominal (n = 3).⁹ Selection criteria included a clearly defined, discrete focal area of pain with a neuropathic component or combined somatic/neuropathic pain component with characteristics of burning and increased sensitivity, and failure to respond to other conservative treatments, including medications, psychological therapies, physical therapies, surgery, and pain management programs. Outcomes, assessed at a mean of 8.1 months after implantation (range, 1-23 months), included a combination of numeric pain scores, self-report questionnaires, and patient medical histories. For the entire cohort, pain decreased from 7.4 at baseline to 4.2 at follow-up. Pain scores improved by 75% or more in 34% of patients and by 50% or more in 69% of patients. Analgesia use decreased in 40% of patients after peripheral subcutaneous field stimulation. Adverse events were reported in 14% of patients and included unpleasant sensations, lead erosions, and lead or battery migration.

Verrills et al (2014) also reported on PSFS for chronic headache conditions.¹⁰ After a trial stimulation period, 60 patients underwent permanent implantation of the PSFS system and were followed for an average of 12.9 months (range, 3-42 months). Ten patients required revision of the implant system. Significant reductions in pain from baseline were reported (p≤0.001). Additionally, use of analgesics or prophylactic medications was reduced in 83% of patients, and reductions in degree of disability and depression were noted.

**SUMMARY OF EVIDENCE**

For individuals who have chronic neuropathic pain who receive peripheral nerve stimulation (PNS) therapy, the evidence is limited to a small number of randomized controlled trials and case series that suggests implantable PNS is safe and works as intended to treat chronic pain or peripheral nerve origin. However, results need confirmation in additional randomized controlled trials with longer follow-up to draw conclusions on safety and efficacy. Further studies should also compare implantable PNS with other neurostimulation therapy such as spinal cord stimulation and alternative treatments. The evidence is insufficient to determine the effects of this technology on net health outcomes.

For individuals who have chronic neuropathic pain who receive peripheral subcutaneous field stimulation (PSFS), the evidence includes a RCT, a nonrandomized comparative study, and case series. Relevant outcomes are symptoms, quality of life and treatment-related morbidity. The single RCT, which used a crossover design, did not compare PSFS with alternatives. Rather it compared different methods of PSFS. Among trial participants, 24 (80%) of 30
patients had at least 50% reduction in pain with any type of PSFS. However, because the RCT did not include a sham group or comparator with a different active intervention, this trial offers little evidence for efficacy beyond that of a prospective, uncontrolled study. Case series are insufficient to evaluate pain outcomes due to the variable nature of pain and the subjective nature of pain outcome measures. Prospective controlled trials comparing PSFS with placebo or alternative treatment modalities are needed to determine the efficacy of PSFS for chronic pain. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Ongoing and Unpublished Clinical Trials**

Some currently unpublished trials that might influence this review are listed in Table 1.

**Table 1. Summary of Key Trials**

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<td>NCT02893267</td>
<td>Multimodal treatment for hemiplegic shoulder pain</td>
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<td>The SNAP trial: SPRINT peripheral nerve stimulation for the treatment of neuropathic post-amputation pain in a randomized, double-blinded, placebo-controlled multicenter trial</td>
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<td>NCT03752619</td>
<td>Peripheral nerve stimulation (PNS) for subacromial impingement syndrome (SIS)</td>
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<td>NCT04246281</td>
<td>SPRINT® peripheral nerve stimulation for the treatment of back pain</td>
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<td>NCT04670042</td>
<td>Using PNS to treat chronic post-surgical pain after knee surgery</td>
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NCT: national clinical trial; ISRCTN: international standard RCT number

**SUPPLEMENTAL INFORMATION**

**Practice Guidelines and Position Statements**

The National Institute for Health and Care Excellence (NICE) issued guidance (2013) on peripheral subcutaneous field stimulation for chronic low back pain, which stated:11

“Current evidence on the efficacy of peripheral nerve-field stimulation for chronic low back pain is limited in both quantity and quality, and duration of follow-up is limited. Evidence on safety is also limited and there is a risk of complications from any implanted device.”
Government Regulations
National:

NCD (160.7) effective 08/07/1995. "Payment may be made under the prosthetic device benefit for implanted peripheral nerve stimulators. Use of this stimulator involves implantation of electrodes around a selected peripheral nerve. The stimulating electrode is connected by an insulated lead to a receiver unit which is implanted under the skin at a depth not greater than 1/2 inch.

"Stimulation is induced by a generator connected to an antenna unit which is attached to the skin surface over the receiver unit. Implantation of electrodes requires surgery and usually necessitates an operating room.
"Peripheral nerve stimulators may also be employed to assess a patient's suitability for continued treatment with an electric nerve stimulator."

Local:
There is no local coverage determination (LCD) on this topic.

(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

• Interferential Stimulation
• Neuromuscular Electrical Stimulation
• Occipital Nerve Stimulation
• Spinal Cord Stimulation

References


The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through January 2022, the date the research was completed.
# Joint BCBSM/BCN Medical Policy History

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Next Review Date: 1<sup>st</sup> Qtr. 2023
BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: PERIPHERAL SUBCUTANEOUS FIELD STIMULATION AND PERIPHERAL NERVE STIMULATION

I. Coverage Determination:

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II. Administrative Guidelines:

N/A