Implantable Peripheral Nerve Stimulation for the Treatment of Chronic Pain

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DESCRIPTION

Implantable peripheral nerve stimulation (StimRouter and ReActiv8) for chronic pain of peripheral nerve origin is a type of neuromodulation therapy that involves the surgical implantation of electrodes that target peripheral nerves considered to be the origin of pain. This procedure differs from other forms of electrical stimulation, because of the origin of pain is from a peripheral nerve and the electrical impulses are delivered to the nerve versus surrounding tissues or the spine.

Implantable peripheral nerve stimulation varies from other electrical stimulation therapies:

- Spinal cord stimulation (SCS) delivers electrical impulses to the spine versus directly to the peripheral nerve pain site.

- Transcutaneous electrical nerve stimulation (TENS) delivers pulses below the skin, to alleviate pain.
- Percutaneous electrical nerve stimulation (PENS) is similar to TENS, except PENS requires electrodes to be inserted into the skin.
- Percutaneous neuromodulation therapy (PNT) is similar to PENS, but PNT is an electrical stimulation therapy using very thin needle electrodes that are inserted directly into the deep tissues in the area causing pain.
- Peripheral subcutaneous field stimulation (PSFS) is electrical stimulation via electrodes placed subcutaneously under the skin over the area of maximal pain. similar to TENS.

Chronic pain originating in peripheral nerves has very variable presentation, and often unclear etiology and as a result treatment is challenging. First-line pain management typically involves pharmacotherapy (NSAIDs, steroids, anti-depressants) and physical therapy. However, many patients do not achieve sufficient relief. Second and third-line options include therapeutic injections (epidural steroid injections, nerve blocks, trigger point injections), intrathecal drug pumps to deliver drugs directly to nerve centers and neurostimulation with electric pulses to override pain signals. Implantable peripheral nerve stimulation is being utilized for management of chronic pain of peripheral origin to treat upper/lower limb pain, entrapment syndromes, intercostal neuralgias and other peripheral injuries or diseases.

As with other types of implantable nerve stimulation, implantation of the peripheral nerve stimulator is typically a two-step process. Initially, the electrode is temporarily implanted allowing a trial period of stimulation typically less than 5 days. The temporary electrode is connected to an external power source that the patient controls. Once treatment effectiveness is confirmed, defined as at least 50% reduction in pain, the permanent placement of electrode(s) is implanted, and are connected either to an implanted pulse generator or the implanted electrode responds to a wireless system using an external radiofrequency transmitter.

Clinical Context and Therapy Purpose
The purpose of implantable peripheral nerve stimulation in individuals who have chronic peripheral nerve pain is to provide a treatment option that is an alternative to or an improvement on existing therapies.

Populations
The relevant population of interest is individuals with chronic peripheral nerve pain.

Interventions
The therapy being considered is implantable peripheral nerve stimulation. Implantable peripheral nerve stimulation is a type of neuromodulation therapy that involves the surgical implantation of electrodes that target peripheral nerves considered to be the origin of pain. This procedure differs from other forms of electrical stimulation, because

of the origin of pain is from a peripheral nerve and the electrical impulses are delivered to the nerve versus surrounding tissues or the spine.

Comparators
The following therapies are currently being used to make decisions about implantable peripheral nerve stimulation: pharmacotherapy, exercise or physical therapy, and cognitive-behavioral therapy.

Outcomes
The principal outcomes associated with the treatment of pain due to any cause include the following: relief of pain, improved function, and improved quality of life (QOL). Relief of pain can be a subjective outcome associated with a placebo effect (improvement of the patient's condition simply because the person has the expectation the treatment, they are receiving might be helpful). Therefore, data from adequately powered, blinded, randomized controlled trials (RCTs) are required to determine if an implanted peripheral nerve stimulation system for chronic pain of peripheral nerve origin provides management changes and improves net health outcomes. Studies should also compare peripheral nerve stimulation with other neurostimulation such as spinal cord stimulation and alternative treatments with long term outcomes to assess safety and effectiveness.

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

Review of Evidence Regarding StimRouter

Systematic Reviews
There were no systematic reviews identified.

Case Series
The majority of the literature related to implantable peripheral nerve stimulation for various conditions (e.g., treatment of hemiplegic shoulder pain; peripheral neuropathic pain; intercostal neuralgia; back pain; neck pain; occipital neuralgia; postherpetic neuralgia; and trigeminal neuralgia/trigeminal neuropathic pain) is case series. While case series are appropriate for introducing novel interventions, they have inherent limitations. Results may be generalized, there are no controls, outcomes are not blinded, assessor bias cannot be ruled out, no comparative information to alternative treatments and no long- term follow-up. These case series may show promising results, however, 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 treatment(s) at a comparable intensity with long term follow-up to verify safety and efficacy.

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.

Ongoing Trials

A prospective, multi-center, single-arm study that will include 50 participants to assess StimRouter's effectiveness for treating severe intractable chronic shoulder pain subsequent to stroke. The primary endpoint will be a clinically relevant pain reduction (30%) in pain score at 3 months after initiating stimulation in at least 50% of patients with no increase in pain medication. Expected completion October 2020

(NCT03093935). This study will not provide the data needed to confirm efficacy and safety because it has no control group, and chronic pain waxes and wanes over time, pain is a subjective measure, and single-arm study design will have a high risk of bias so that results cannot be reliably attributed to the intervention. Accessed ClinicalTrials.gov on October 3, 2021, and this clinical trial was terminated due to lack of subject participation.

A prospective open label long term multicenter registry to evaluate the long-term effectiveness, safety, and tolerability of the StimRouter Neuromodulation System, along with evaluating the technical performance of StimRouter, surgical outcomes, health-related quality of life, concomitant medical use and subject's impression of improvement. The primary endpoints are change in numeric pain rating scale, number of subjects with adverse events, vital signs including height, weight, heart rate and blood pressure, physical and neurological exams through 60-months post-implant. Expected completion is April 2028 (NCT03913689).

Summary of Evidence
Based on review of the peer reviewed medical literature regarding StimeRouter the evidence is limited to a small number of randomized controlled trials and case series that suggests implantable peripheral nerve stimulation is safe and works as intended to treat chronic pain of peripheral nerve origin. However, results need confirmation in additional randomized controlled trials (RCTs) with longer follow-up to draw conclusions on safety and efficacy. Further studies should also compare implantable peripheral nerve stimulation with other neurostimulation therapy such as spinal cord stimulation and alternative treatments. Currently there are no evidence based clinical practice guidelines that recommend the use of implantable peripheral nerve stimulation for the treatment of chronic pain of peripheral nerve origin. The evidence is insufficient to determine the effects of this technology on net health outcomes.

Review of Evidence Regarding ReActiv8
Hayes Evolving Evidence Review completed May 2022 regarding ReActiv8 implantable neurostimulation system for chronic low back pain includes randomized controlled trials (RCTs) which may have shown some promise regarding improvement in pain, disability and quality of life (QOL), however, no studies compared ReActive8 with an active comparator and several serious adverse events were reported, mild and moderate adverse events were common some of which required a need for revision surgery and reimplantation. There were no professional society guidelines found addressing the use of ReActive8 in the treatment of chronic low back pain (CLBP). No systematic reviews were found. There are ongoing clinical trials and should be monitored for additional follow-up data.

The ReActiv8 Implantable Peripheral Neurostimulation System includes an implantable pulse generator (IPG), 2 stimulation leads, a magnet, and a wireless remote. The IPG delivers electrical stimulation pulses to certain nerves responsible for activating the lumbar multifudus muscle, the key muscles responsible for stabilizing the lower back. It is intended to help with the management of chronic low back pain (LBP) associated with

the muscular weakness of the lumbar multifidus muscle in patients who have failed therapy including pain medications and physical therapy and are not candidates for spine surgery. Before implanting the device, multifudus muscle atrophy and weakness must be shown using magnetic resonance imaging (MRI) or during a physical examination using the prone instability test.

In 2021, Mitchell et. al. reported the 4-year outcomes of the ReActiv8-A Trial. Eligible patients had disabling chronic low back pain (CLBP), no indications for spine surgery or spinal cord stimulation (SCS) and failed conventional management including at least physical therapy (PT) and medications for low back pain (LBP). Fourteen days post-implantation, stimulation parameters were programmed to elicit strong, smooth contractions of the multifidus, and subjects were given instructions to activate the device for 30-min stimulation-sessions twice-daily. Annual follow-up through 4 years included collection of NRS, ODI, and European QOL Score on 5 Dimensions (EQ-5D). At baseline (n = 53) (mean ± SD) age was 44 ± 10 years; duration of back pain was 14 ± 11 years, NRS was 6.8 ± 0.8, ODI 44.9 ± 10.1, and EQ-5D 0.434 ± 0.185. Mean improvements from baseline were statistically significant ($p < 0.001$) and clinically meaningful for all follow-ups. Patients completing year 4 follow-up, reported mean (± standard error of the mean) NRS: 3.2 ± 0.4, ODI: 23.0 ± 3.2, and EQ-5D: 0.721 ± 0.035. Moreover, 73 % of subjects had a clinically meaningful improvement of greater than or equal to 2 points on NRS, 76 % of greater than or equal to 10 points on ODI, and 62.5 % had a clinically meaningful improvement in both NRS and ODI and 97 % were (very) satisfied with treatment. The authors concluded that in patients with disabling intractable CLBP who receive long-term restorative neurostimulation, treatment satisfaction remains high; pain and disability in the 4-year completed case cohort were on average 53 % and 50 % lower than baseline, respectively, suggesting that the effects were durable over the long-term. Moreover, these researchers stated that the longitudinal analysis presented was not without limitations. After 4 years, 19/53 (35.9 %) patients were missing data for various reasons. Furthermore, the relatively high lead revision rate that contributed to early attrition may also have impacted reported outcomes.

In 2021, Galligan et. al. performed a randomized, double-blind, sham-controlled trial at 26 multi-disciplinary centers to determine the safety and effectiveness of an implantable, restorative neurostimulator designed to restore multifidus neuromuscular control and facilitate relief of symptoms. A total of 204 eligible subjects with refractory mechanical CLBP and a positive prone instability test indicating impaired multifidus control were implanted and randomized to therapeutic (n = 102) or low-level sham (n = 102) stimulation of the medial branch of the dorsal ramus nerve (multifidus nerve supply) for 30 mins twice daily. The primary endpoint was the comparison of responder proportions (greater than or equal to 30 % relief on the LBP-VAS without analgesics increase) at 120 days. After the primary endpoint assessment, subjects in the sham-control group switched to therapeutic stimulation and the combined cohort was evaluated through 1 year for long-term outcomes and AEs. The primary endpoint was inconclusive in terms of treatment superiority (57.1 % versus 46.6 %; difference: 10.4 %; 95 % confidence interval [CI]: -3.3 % to 24.1 %, p = 0.138). Pre-specified secondary outcomes and

analyses were consistent with a modest but clinically meaningful treatment benefit at 120 days. Improvements from baseline, which continued to accrue in all outcome measures after conclusion of the double-blind phase, were clinically important at 1 year. The incidence of serious procedure- or device-related AEs (3.9 %) compared favorably with other neuromodulation therapies for chronic pain. The authors concluded that this double-blind, randomized, sham-controlled trial provided important insights and design considerations for future neuromodulation trials. Although the primary endpoint was inconclusive, overall data from the blinded phase of this trial were consistent with a clinically meaningful benefit at 120 days. After unblinding and the switch from sham to therapeutic stimulation in the sham-control group, improvements increased over time out to 1 year in the combined cohort. The incidence of serious procedure- or device-related AEs compared favorably with rates published for other neuromodulation therapies for chronic pain. Follow-up of subjects in this trial will continue for a total of 5 years, providing additional insights into the long-term benefits, risks, and reliability of this device. There were several drawbacks that need to be addressed when interpreting the findings in this study. First, at the time of trial design, the size and duration of the sham response to this type of treatment in subjects with CLBP was unknown. The statistical design assumptions, derived from a literature review for available CLBP treatments, under-estimated the response to a surgically implanted active sham device. Although the LBP-VAS trajectory suggested that the sham effect may be reversing at 120 days, due to the pre-specified switch of the sham-control group to therapeutic stimulation, these investigators were unable to confirm this longer term. Second, although previous studies had shown that observed improvements with this rehabilitative treatment accrue over time, endpoint timing was set to 120 days for practical and ethical reasons, and the fixed 30 % threshold for pain relief reflected the expected improvement at 120 days rather than the fully accrued long-term treatment effect. Finally, although sham stimulation parameters were set to low amplitude and frequency values, a potential therapeutic effect could not be ruled out and this might have diminished the magnitude of the group differences in the outcome measures.

Galligan et. al. (2021) The ReActiv8-B randomized, active-sham-controlled trial provided safety and effectiveness evidence for this device, and all subjects received therapeutic stimulation from 4 months onward. These authors examined the 2-year effectiveness of this restorative neurostimulator in patients with disabling CLBP secondary to multifidus muscle dysfunction and no indications for spine surgery. Open-label follow-up of 204 subjects implanted with a restorative neurostimulation system (ReActiv8) was carried out. Pain intensity (VAS), disability (ODI), QOL (EQ-5D-5L), and opioid intake were examined at baseline, 6 months, 1 year, and 2 years after activation. At 2 years (n = 156), the proportion of subjects with greater than or equal to 50 % CLBP relief was 71 %, and 65 % reported CLBP resolution (VAS less than or equal to 2.5 cm); 61 % had a reduction in ODI of greater than or equal to 20 points, 76 % had improvements of greater than or equal to 50 % in VAS and/or greater than or equal to 20 points in ODI, and 56 % had these substantial improvements in both VAS and ODI. A total of 87 % of subjects had continued device use during the 2nd year for a median of 43 % of the maximum duration, and 60 % (34 of 57) had voluntarily discontinued (39 %) or

reduced (21 %) opioid intake. The authors concluded that at 2 years, 76 % of participants experienced substantial, clinically meaningful improvements in pain, disability, or both. These results provided evidence of long-term effectiveness and durability of restorative neurostimulation in patients with disabling CLBP, secondary to multifidus muscle dysfunction. However, the authors stated that the main drawback of this study was the absence of a long-term comparator because of therapy activation in the sham-control group after conclusion of the blinded phase at 4 months. Furthermore, studies with long follow-up durations will inherently have to account for missing data, especially those for chronic pain conditions. Indiscriminate use of last observation carried forward has been criticized as a source of systematic bias in chronic pain trials, and more appropriate methods have been recommended.

Furthermore, there is an ongoing clinical trial on "ReActiv8 Implantable Neurostimulation System for Chronic Low Back Pain (ReActiv8-B)" with an estimate study completion date of December 2023.

In 2021, Provenzano et. al. stated that neurostimulation techniques for the treatment of chronic LBP have been rapidly evolving; however, questions remain as to which modalities provide the most effective and durable treatment for intractable axial symptoms. Modalities of spinal cord stimulation (SCS), such as traditional low-frequency paresthesia based, high-density or high dose (HD), burst, 10-kHz high-frequency therapy, closed-loop, and differential target multiplexed, have been limitedly studied to determine their efficacy for the treatment of axial LBP. Furthermore, stimulation methods that target regions other than the spinal cord, such as medial branch nerve stimulation of the multifidus muscles and the dorsal root ganglion (DRG) may also be viable therapeutic options. The authors concluded that the minimal invasiveness of neurostimulation remains a compelling reason for patients to seek this therapeutic option for the treatment of axial LBP. Invasive surgical methods (e.g., fusion) that alter the anatomy of the spine with considerable rates of failure and high AEs rates are often considered before neurostimulation. These researchers stated that if neurostimulation is shown to demonstrate long-term effectiveness in appropriately designed RCTs with low complication and explant rates, then neurostimulation therapies may move up in the treatment algorithm for chronic axial LBP and refractory non-surgical LBP.

In 2018, Deckers et. al. in a prospective, single-arm, multi-center clinical trial, examined restorative neurostimulation eliciting episodic contraction of the lumbar multifidus for treatment of chronic mechanical LBP (CMLBP) in patients who have failed conventional therapy and are not candidates for surgery or spinal cord stimulation (SCS). A total of 53 subjects were implanted with a neurostimulator (ReActiv8, Mainstay Medical Limited, Dublin, Ireland). Leads were positioned bilaterally with electrodes close to the medial branch of the L2 dorsal ramus nerve. The primary outcome measure was LBP evaluated on a 10-point numerical rating scale (NRS). Responders were defined as subjects with an improvement of at least the Minimal Clinically Important Difference (MCID) of greater than or equal to 2-point in LBP NRS without a clinically meaningful increase in LBP medications at 90 days. Secondary outcome measures included Oswestry Disability

Index (ODI) and QOL (EQ-5D). For 53 subjects with an average duration of CLBP of 14 years and average NRS of 7 and for whom no other therapies had provided satisfactory pain relief, the responder rate was 58 %. The percentage of subjects at 90 days, 6 months, and 1 year with greater than or equal to MCID improvement in single day NRS was 63 %, 61 %, and 57 %, respectively. Percentage of subjects with greater than or equal to MCID improvement in ODI was 52 %, 57 %, and 60 % while those with greater than or equal to MCID improvement in EQ-5D was 88 %, 82 %, and 81 %. There were no unanticipated AEs or serious AEs related to the device, procedure, or therapy. The initial surgical approach led to a risk of lead fracture, which was mitigated by a modification to the surgical approach. The authors concluded that electrical stimulation to elicit episodic lumbar multifidus contraction is a new therapeutic option for CMLBP; results demonstrated clinically important, statistically significant, and lasting improvement in pain, disability, and QOL. However, this study had several drawbacks. First, it did not include a control arm. Second, the primary outcome measure in this study was improvement in pain evaluated with the NRS; however, evaluating changes in multiple outcome measures may be more clinically relevant (e.g., many trials of spine surgery for LBP used a composite outcome measure including assessment of disability). Third, lead issues that resulted in loss of stimulation for a period of time may have negatively impacted the outcomes in the affected subjects. Fourth, outcome data to 1 year were presented. Subjects in this study will continue to be evaluated annually through 5 years as part of a post-market clinical follow-up study, which will provide information on longer term safety and efficacy. Finally, the data from this trial have not been analyzed to examine patient parameters that could be predictive of outcomes, and further research is needed to more clearly identify the best candidates for this therapy.

Summary of Evidence

Based on review of the peer reviewed medical literature regarding ReActive8 the evidence is limited to randomized controlled trials (RCTs) and no systematic reviews. While randomized controlled trials may have shown promise regarding improvement in pain, disability, and quality of life (QOL), there were no studies that compared ReActive8 with an active comparator and there were several serious adverse events reported to include mild and moderate adverse events which were common some of which required a need for revision surgery and reimplantation. There are currently no professional society guidelines found addressing the use of ReActive8 in the treatment of chronic low back pain (CLBP). Further comparative studies with longer follow-up are needed, there is an ongoing clinical trial on "ReActiv8 Implantable Neurostimulation System for Chronic Low Back Pain (ReActiv8-B)" with an estimate study completion date of December 2023. Currently, there is insufficient evidence to support the use of the Reactiv8 device for the treatment of chronic LBP.

Practice Guidelines and Position Statements

Currently there are no evidence based clinical practice guidelines that recommend the use of implanted peripheral nerve stimulation (StimRouter or ReActiv8) for the treatment of pain of peripheral nerve origin and the treatment of chronic low back pain.

Regulatory Status
In February 2015 the U.S. Food and Drug Administration (FDA) granted 510(k) marketing clearance for the StimRouter Neuromodulation System (Bioness, Inc., Valencia, CA). The StimRouter Neuromodulation System is indicated for pain management in adults who have severe intractable pain of peripheral nerve origin, as an adjunct to other modes of therapy (i.e.., medications). The StimRouter is not intended to treat pain in the craniofacial region.

Patient Components

- StimRouter Lead: The StimRouter Lead is flexible and approximately 15 cm (6 inches) in length. The lead had a stimulation end and a receiver end. The stimulation end is implanted near or at the targeted peripheral nerve and the receiver end is implanted new the skin surface. The receiver end receives the stimulation signal from the external pulse transmitter (EPT) and then send the signal through the lead to the stimulation end.
- StimRouter External Pulse Transmitter (EPT): The StimRouter EPT generates the stimulation signal and transmits the signal through the StimRouter Electrode to the StimRouter Lead. The EPT snaps onto the StimRouter Electrode and responds to wireless commands from the Patient Programmer.
- StimRouter Electrode: The StimRouter Electrode features:
    - Two gel pads that adhere the StimRouter Electrode to the skin. The gel pads also transmit the stimulation signal from the EPT to the receiver end of the lead.
    - Two snaps for EPT placement.
    - Two tabs for removing the StimRouter Electrode from the skin.
    - A liner to protect the gel pads on the back of the StimRouter Electrode.
    - The StimRouter Electrode is disposable and can be reused by the same patient as long as the gel pads are intact and can fully adhere to the skin or for a maximum of four days of use.
    - The typical lifespan of the StimRouter Electrode is two to four days depending on:
        - The number of hours of use.
        - The number of times the StimRouter Electrode is adhered and removed from the skin.
        - Hygiene and skin care in the area of StimRouter Electrode placement.
- Patient Programmer: The Patient Programmer communicates wirelessly with the EPT (external pulse transmitter). The Patient Programmer is used to turn stimulation on and off, to adjust the stimulation intensity and to select a stimulation program.

In March 2016 the U.S. Food and Drug Administration (FDA) granted 510(k) marketing clearance for the StimQ Peripheral Nerve Stimulator (PNS) System (Stimwave LLC, Pompano Beach, FL). The StimQ Peripheral Nerve Stimulator (PNS) System 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 therapy utilizes pulsed electrical current to create an electrical energy field that acts on peripheral nerves in the limbs and torso to alter transmission of pain signals to the brain. 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.

Device Description:

- The system is comprised of an implantable stimulator and an externally worn transmitter (StimQ Wearable Antenna Gear (SWAG)) to power the device. The system is implanted only following a successful trial period with the trial lead.

In August 2017, the U.S. Food and Drug Administration (FDA) granted 510(k) marketing clearance for StimQ wireless peripheral nerve stimulator system. This device can be placed minimally invasive, provides pain relief by delivering small pulses of energy to electrodes placed at a peripheral nerve enabling the brain to remap the pain signals. The implant is powered by a small external unit.

In June 2020, the U.S. Food and Drug Administration (FDA) granted 510(k) marketing clearance for ReActiv8 Implantable Neurostimulation System. This device is indicated for the following: The ReActiv8 Implantable Neurostimulation System is intended to help with the management of chronic low back pain associated with the muscular weakness of the lumbar multifidus muscle in patients who have failed therapy including pain medications and physical therapy and are not candidates for spine surgery.

PRIOR APPROVAL

Not applicable.

POLICY

See related medical policies

- 01.01.23 Electrical Stimulation for the Treatment of Muscle Rehabilitation, Pain and Miscellaneous
- 07.01.61 Spinal Cord and Dorsal Root Ganglion Stimulation
- 07.01.70 Peripheral Subcutaneous Field Stimulation (PSFS)

Implantable peripheral nerve stimulation (StimRouter or ReActive8) including the temporary and permanent placement for the management of chronic pain of peripheral origin is **investigational** for all indications including but not limited to the following,

because the evidence is insufficient to determine the effects of this technology on net health outcomes:

- Chronic shoulder pain subsequent to stroke
- Entrapment syndromes
- Intercostal neuralgia
- Chronic Low back pain
- Neck pain
- Neuropathic craniofacial pain
- Occipital neuralgia
- Painful nerve injuries
- Painful peripheral neuropathies
- Peripheral vascular disease neuropathy
- Post herpetic neuralgia
- Trigeminal neuralgia
- Trigeminal neuropathic pain

PROCEDURE CODES AND BILLING GUIDELINES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnosis codes.

- 64555 percutaneous implantation of neurostimulator electrode array; peripheral nerve
- 64575 Open implantation of neurostimulator electrode array; peripheral nerve (excludes sacral nerve)
- 64585 revision or removal of peripheral neurostimulator electrode array
- 64590 insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling
- 64595 revision or removal of peripheral or gastric neurostimulator pulse generator or receiver
- 95970 Electronic analysis of implanted neurostimulator pulse generator/transmitter (e.g., contact group(s), interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with brain, cranial nerve, spinal cord, peripheral nerve, or sacral nerve, neurostimulator pulse generator/transmitter, without programming
- 95971 Electronic analysis of implanted neurostimulator pulse generator/transmitter (e.g., contact group(s), interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with

simple spinal cord or peripheral nerve (e.g., sacral nerve) neurostimulator pulse generator/transmitter programming by physician or other qualified health care professional

- 95972 Electronic analysis of implanted neurostimulator pulse generator/transmitter (e.g., contact group(s), interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with complex spinal cord or peripheral nerve (e.g., sacral nerve) neurostimulator pulse generator/transmitter programming by physician or other qualified health care professional
- C1767 Generator neurostimulator (implantable) non-rechargeable
- C1778 Lead, neurostimulator
- C1787 Patient programmer, neurostimulator
- C1816 Receiver and/or transmitter neurostimulator (implantable)
- C1820 Generator, neurostimulator (implantable), non-high frequency with rechargeable battery and charging system
- C1822 Generator, neurostimulator (implantable), high frequency, with rechargeable battery and charging system
- C1897 Lead neurostimulator test kit (implantable)
- L8679 Implantable neurostimulator, pulse generator any type
- L8680 Implantable neurostimulator electrode, each
- L8681 Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
- L8682 Implantable neurostimulator radiofrequency receiver
- L8683 Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver
- L8685 Implantable neurostimulator pulse generator, single array, rechargeable includes extension
- L8686 Implantable neurostimulator pulse generator, single array, nonrechargeable, includes extension
- L8687 Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
- L8688 Implantable neurostimulator pulse generator, dual array, nonrechargeable, includes extension
- L8689 External recharging system for battery (internal)for use with implantable neurostimulator, replacement only

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POLICY HISTORY

Date	Reason	Action
October 2022	Annual Review	Policy Revised
October 2021	Annual Review	Policy Renewed
October 2020	Annual Review	Policy Renewed
October 2019	Annual Review	Policy Renewed
October 2018		New Policy Created

New information or technology that would be relevant for Wellmark to consider when this policy is next reviewed may be submitted to:

Wellmark Blue Cross and Blue Shield
Medical Policy Analyst
PO Box 9232
Des Moines, IA 50306-9232

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