



ReActiv8 Implantable Neurostimulation System

Spine, Pain, and Joint (SPJ) Utilization Management Policy

Effective Date: 06/13/2024

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Policy Statement

The ReActiv8 Implantable Neurostimulation System would be considered unproven and not medically necessary for patients with chronic mechanical low back pain due to lumbar multifidus muscle dysfunction. There is insufficient evidence to determine the efficacy of the ReActiv8 system for improving net health outcomes.

For Medicare beneficiaries, refer first to any relevant local coverage determinations (LCDs) and then to the Medicare Benefit Policy Manual, section 16.20, for services considered not reasonable and necessary. [Medicare Benefit Policy Manual \(cms.gov\)](#)

Background Information

The ReActiv8 Implantable Neurostimulation System by Mainstay Medical, Ltd. is an implanted nerve stimulation system that activates the lumbar multifidus muscles of the lower back. For patients with chronic mechanical low back pain who are not candidates for spine surgery and who have failed optimal medical management, stabilization of the lower back may assist in relieving their pain. If clinical examination (e.g., positive prone instability test) and low back imaging (e.g., MRI) confirm multifidus muscle dysfunction is causing muscle weakness and spine instability, this system is purported to restore motor control and muscle function by stimulation of the medical branch of the dorsal ramus nerve when used for two 30-minute sessions daily. This system differs from other neurostimulators that block pain by sensory nerve stimulation.

In June 2020, the ReActiv8 Implantable Neurostimulation System (Mainstay Medical, Ltd.) (P190021) received premarket approval by the FDA. The indication for the ReActiv8 neurostimulator is noted as “bilateral stimulation of the L2 medial branch of the dorsal ramus as it crosses the transverse process at L3 as an aid in the management of intractable chronic low back pain associated with multifidus muscle dysfunction, as evidenced by imaging or physiological testing in adults who have failed therapy including pain medications and physical therapy and are not candidates for spine surgery.” This system includes an implanted pulse generator, two stimulation leads, four electrodes and a handheld battery operated patient activator that communicates with the pulse generator.

An ongoing prospective, randomized clinical trial (NCT04803214) is comparing the ReActive8 stimulation therapy to optimal medical management in patients with chronic low back pain due to lumbar multifidus muscle dysfunction (n=228). Estimated completion is noted to be July 2025.

Clinical Evidence

Gilligan et al (2021) performed a double-masked, multicenter, randomized, controlled trial which compared the ReActiv8 system (n=102) to sham treatment (n=108) with 120-day follow-up. ReActiv8 treatment was provided twice daily in 30-minute sessions. At 120-day follow-up, the sham cohort crossed over and their system was reprogrammed to deliver therapeutic stimulation. No statistical difference was identified in analgesic use or at least 30% pain reduction between the ReActiv8 cohort and sham cohort at 120-day follow-up. Three patients in the ReActiv8 group and nine in the sham group increased their use of analgesics due to chronic low back pain. Six patients in the ReActiv8 cohort increased their analgesic use for etiologies unrelated to their low back pain. The ReActiv8 cohort reported more improvement in Oswestry Disability Index (ODI) scores than the sham group. Quality of life per European Quality of Life 5-Dimension (EQ-5D) scores was reported as better-quality in the ReActiv8 cohort than sham. Although the researchers reported ReActiv8 to be superior to sham in all responder metrics, the primary endpoint did not appear to meet statistical significance.

In 2023, Gilligan et al analyzed the before-and-after data from the study noted above and compared VAS pain scores, ODI changes, EQ-5D changes, opioid use and adverse events in this same cohort. At three-year follow-up, 149 patients remained active in the trial. It was reported 77% of patients experienced >50% pain reduction and 62% reported >70% pain reduction with VAS improved from 7.3±0.7 at baseline to 2.4±0.2. Of the 38% of patients that required opioids at baseline, 71% were reported to have reduced or discontinued their medication, ODI scores were reported as improved by >20 points, and EQ-5D scores improved by 0.22±0.186 from baseline to 3-year follow-up. Six patients had their device explanted because they felt treatment was no longer necessary due to pain relief. Clinically substantial improvements in pain, disability or both were reported in 83% of the patients at three years.

Ardeshiri et al (2022) performed a consecutive cohort study evaluating patients pre- and post-ReActiv8 treatment (n=44). At one-year follow-up, 30 patients experienced ≥30% low back pain reduction and 23 experienced ≥50% pain

reduction. ODI was reported as improved by >10 points in 74% of patients and >20 points in 55% of patients at 1-year follow-up. Quality of life per EQ-5D scores was reported as improved from 0.466±0.04 to 0.770± at 1-year follow-up.

Mitchell et al (2021) evaluated the effect of ReActiv8 treatment at 4-year follow-up (n=53). Outcomes assessed included pain, ODI, EQ-5D, patient satisfaction, and device explantation. From baseline to four-year follow-up, 73% of patients experienced ≥2 points of change on the numeric rating scale (NRS) for pain, improving from 6.7±1.2 at baseline by 3.5, ODI scores improved by ≥10 points in 76% of patients, and EQ-5D scores improved by 0.285. Four patients had their system explanted and felt they no longer needed treatment for their low back pain.

A prospective multicenter, longitudinal cohort study by Thomson et al (2021) compared pain, ODI, and EQ-5D from baseline two years following ReActiv8 treatment (n=42). Thirty-seven patients completed the study. At two-year follow-up, the researchers reported 57% of patients experienced >50% pain reduction and NRS scores improved from 7.0±0.2 from baseline to 3.5±0.3 at two-year follow-up. EQ-5D scores improved from 0.426±0.035 at baseline to 0.680±0.030 at 2-year follow-up. No serious adverse events were reported.

A 2023 Clinical Evidence Assessment by ECRI indicates there are clinical evidence limitations in the before-an-after studies which have been performed on ReActiv8 due to a high risk of bias because of the lack of control groups and/or a single-center focus. The 2023 RCT by Gilligan et al also may have included a different patient population at 3-year follow-up than the original selected patient cohort due to crossover. This assessment indicates additional independent studies which address outcomes in the general population are required in order to substantiate prior study conclusions. Confidence in the clinical evidence for pain relief, disability and quality of life is noted as very low.

Hayes published a 2022 Evolving Evidence Review on the ReActiv8 Implantable Neurostimulation System. This review included evidence from one poor-quality pretest-posttest study and one fair-quality RCT which suggest the ReActiv8 system may offer some clinically significant and statistically significant improvement in disability, pain and quality of life. The authors did not identify any comparative studies evaluating the ReActiv8 system with other peripheral nerve stimulators, any systematic reviews, or any guidelines which directly addressed this system.

A 2022 guideline by the National Institute for Health and Care Excellence (NICE) indicates the evidence on the safety and efficacy of lumbar muscle neurostimulation for treatment of refractory chronic low back pain is limited in quality and quantity. Additional randomized, controlled trials that compare lumbar muscle neurostimulation to the current best practice should be performed. Long-term outcomes and details regarding patient selection should be reported in these additional studies.

Coding Information

Code	Description
Per the manufacturer, possible CPT procedure codes for ReActiv8 may include:	
64999	Unlisted procedure, nervous system
64555	Percutaneous implantation of neurostimulator electrode array; peripheral nerve (excludes sacral nerve)
64590	Insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling
76000	Fluoroscopy, up to one hour- professional component
64585	Revision or removal of peripheral neurostimulator electrode array
64595	Revision or removal of peripheral or gastric neurostimulator pulse generator or receiver
95970	Analysis
95971	Analysis w/simple programming

95972

Analysis w/complex programming

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Review and Approval History

Date	Description
6/12/2024	New policy developed. Approved by Optum Clinical Guideline Advisory Committee.
6/13/2024	Approved by OrthoNet Quality Improvement Committee (QIC).
