Vagus nerve stimulation for post-stroke upper limb rehabilitation

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Next review date: 10/2026

Policy contains: Rehabilitation; stroke; upper limb; vagus nerve stimulation; Vivistim.

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Coverage policy

Vagus nerve stimulation as an adjunct to rehabilitation in members with upper limb impairment after stroke is investigational/not clinically proven and, therefore, not medically necessary.

Limitations

No limitations were identified during the writing of this policy.

Alternative covered services

Guideline-directed stroke rehabilitation services.

Background

Stroke is a leading cause of serious long-term disability. In the United States, stroke occurs in an estimated 800,000 people annually, and approximately two-thirds survive and require rehabilitation. Upper limb impairment

is a common consequence, resulting in paresis, abnormal muscle tone, sensory disturbances, and reduced coordination (Tsao, 2022). Up to 22% of patients experience shoulder pain associated with shoulder subluxation and motor weakness in the first year following stroke (Winstein, 2016).

Customized rehabilitation applies focused, repetitive practice to maximize residual function, level of independence, and quality of life. Recovery targets the surviving brain tissue with the goal of promoting neural repair (National Institute of Neurological Disorders and Stroke, 2023). Treatments in stroke recovery are considered nonvascular, both pharmacological and nonpharmacological, and are initiated in the subacute to chronic phases (days to years) after stroke (Lin, 2018).

Conventional interventions used in stroke recovery include physical, occupational, and speech therapy. Electrical neurostimulation has been proposed as adjunctive treatment to enhance recovery. Novel invasive approaches, such as transcranial magnetic stimulation and deep brain stimulation, target post-stroke deficits such as motor, language, memory, and neglect (Lin, 2018). Transcutaneous electrical nerve stimulation and neuromuscular electrical stimulation have been studied for treating hemiplegic shoulder pain, albeit with limited success (Winstein, 2016).

Vagus nerve stimulation represents a novel, drug-free, adjunctive treatment in stroke recovery for regaining upper extremity motor function. Its mechanism of action is not completely understood, but preclinical research suggests it modulates irregular electrical activity in the brain, thereby enhancing brain plasticity (Lin, 2018).

The U.S. Food and Drug Administration (2021) has granted premarket approval to one implantable vagus nerve stimulator for commercial use as a breakthrough technology designation: The MicroTransponder® Vivistim® Paired VNS System (MicroTransponder, Inc., Austin, Texas). Vivistim consists of a pulse generator implanted in the pectoral region, a lead electrode attached to the left vagus nerve in the neck, a wireless transmitter, and software. Vivistim is indicated for stimulation of the vagus nerve during rehabilitation therapy to reduce upper extremity motor deficits and improve motor function in patients with chronic ischemic stroke and moderate to severe arm impairment.

No transcutaneous vagus nerve stimulators have been approved for this indication (U.S. Food and Drug Administration, 2025).

Findings

Clinical Guidelines

Clinical guidelines offer limited but evolving support for vagus nerve stimulation as an adjunctive therapy in stroke rehabilitation, particularly for improving upper extremity function. The guideline from the American Heart Association and American Stroke Association notes that evidence for most stroke rehabilitation interventions, including those targeting upper extremity improvements, remains mixed or incomplete, without directly addressing vagus nerve stimulation (Winstein, 2016).

A 2024 guideline from the Department of Veterans Affairs and Department of Defense provides the clearest stance on vagus nerve stimulation. It concludes that pairing vagus nerve stimulation with task-specific rehabilitation may enhance motor recovery by modulating neural networks and increasing neuroplasticity. However, the clinical evidence is limited in quality and scope, with studies often having small sample sizes, potential publication bias, and a focus on short-term rather than long-term outcomes. Interventions involving surgically implanted vagus nerve stimulators carry risks, including postoperative complications, the need for recurrent surgeries to replace batteries, and contraindications common in stroke patients, such as cardiac arrhythmias and sleep apnea. High initial costs and varying patient willingness to undergo invasive procedures further restrict clinical use.

Systematic Reviews and Meta-Analyses

Recent systematic reviews and meta-analyses generally confirm the safety and moderate effectiveness of vagus nerve stimulation for upper limb motor rehabilitation after stroke but highlight persistent uncertainties. Studies by Xie (2021), Ananda (2022), Gao (2023), Liu (2022b), Ramos-Castaneda (2022), and Zhao (2022) collectively conclude that vagus nerve stimulation combined with rehabilitation is feasible, safe, and moderately effective based on available randomized controlled trials. However, these reviews consistently note gaps in evidence concerning long-term functional outcomes, mental health impacts, activities of daily living, and the effects of different patient characteristics and stimulation parameters.

A comprehensive systematic review and meta-analysis by Kalagara (2025) examined complications from implanted vagus nerve stimulators across 21 randomized controlled trials involving (n = 1,474) patients. The review identified the five most common adverse events as voice alteration or hoarseness (45.5%), paresthesia (15.8%), cough (15.0%), dyspnea (14.3%), and pain (11.5%). These complications were generally mild and transient, with both severity and frequency decreasing over time. The review covered vagus nerve stimulation applications for conditions including epilepsy (nine studies), depression (8 studies), anxiety (one study), ischemic stroke (1 study), chronic heart failure (one study), and fibromyalgia (one study). This safety data is critical for informed consent as vagus nerve stimulation is further explored for stroke rehabilitation.

A meta-analysis by Wang (2023) of 10 trials with (n = 335) participants highlighted the potential efficacy of lower-frequency (less than 25 Hz) and noninvasive vagus nerve stimulation for stroke rehabilitation. This study suggests noninvasive approaches may offer benefits comparable to implanted stimulators with fewer procedural risks, calling for additional high-quality research to refine clinical indications, optimize stimulation parameters, and establish standardized methodologies. These findings underscore the promise of both invasive and noninvasive vagus nerve stimulation for post-stroke recovery while emphasizing the need for further investigation into long-term outcomes and tailored treatment protocols.

Primary Clinical Evidence

The primary evidence supporting the clinical efficacy of implanted vagus nerve stimulation comes from a pivotal randomized controlled trial with 108 participants (n = 108) (Dawson, 2021), supported by two earlier pilot studies (Dawson, 2016, 2020; Kimberley, 2018). These studies consistently show statistically significant but modest improvements in motor function when vagus nerve stimulation is combined with conventional rehabilitation compared to rehabilitation alone. Dawson (2021) reported a clinically meaningful response rate of 47% in the stimulation group compared to 25% in controls, with significant improvements in Fugl-Meyer Assessment-Upper Extremity and Wolf Motor Function Test scores at 90 days. However, Kwakkel (2021) cautions that improvements of 2.5 to 3 points on the Fugl-Meyer scale, while statistically significant, may not represent substantial clinical benefits.

Subgroup analyses confirm consistent outcomes across diverse patient demographics, including gender, age, stroke chronicity, baseline severity, paretic side, and country of treatment (Dawson, 2023). The device implantation and stimulation settings (0.8 mA, 30 Hz, 100 ms pulse width) were standardized, with therapy regimens involving six weeks of intensive in-clinic rehabilitation followed by prescribed home therapy. Extended follow-ups indicate sustained motor function improvements and quality-of-life enhancements (Dawson, 2020, 2021).

Safety Evidence

Safety evaluations across clinical trials consistently report that vagus nerve stimulation is generally well-tolerated, with most adverse events being mild to moderate. Dawson (2021) documented 334 adverse events among participants (n = 108), primarily mild, with the most common being pain related to device implantation.

Serious events were rare, with only one transient vocal cord paresis reported, and device removal was mainly due to study discontinuation rather than complications. Surgical adverse event rates for stroke rehabilitation patients were lower compared to those receiving vagus nerve stimulation for epilepsy or depression (Liu, 2022a).

In 2025, we restructured the findings section into distinct sections (clinical guidelines, systematic reviews and meta-analyses, primary clinical evidence, and safety evidence), notably adding the updated 2024 Department of Veterans Affairs/Department of Defense Clinical Practice Guideline and a new systematic review on vagus nerve stimulation (Kalagara, 2025)

References

On May 19, 2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “stroke rehabilitation (MeSH),” “vagus nerve stimulation (MeSH),” “vagus nerve stimulation,” and “stroke.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

6/2022: initial review date and clinical policy effective date: 7/2022

6/2023: Policy references updated.

6/2024: Policy references updated.
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