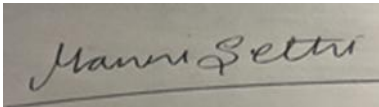


Prior Authorization Review Panel
MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: AmeriHealth Caritas Pennsylvania Community HealthChoices/Keystone First Community HealthChoices		Submission Date: 7/1/2025	
Policy Number: CCP.1515		Effective Date: 7/1/2022 Revision Date: 6/2025	
Policy Name: Vagus nerve stimulation for post-stroke upper limb rehabilitation			
Type of Submission:		Type of Policy:	
☐ New Policy		☒ Prior Authorization Policy	
☒ Revised Policy*		☐ Base Policy	
☐ Annual Review- no revisions		☒ Experimental/Investigational Policy	
		☐ Statewide PDL	
		☐ Other:	
*All revisions to the policy <u>must</u> be highlighted using track changes throughout the document. Please provide any clarifying information for the policy below:			
Name of Authorized Individual (Please type or print): Manni Sethi, MD, MBA, CHCQM		Signature of Authorized Individual: 	

Vagus nerve stimulation for post-stroke upper limb rehabilitation

Clinical Policy ID: CCP.1515

Recent review date: 6/2025

Next review date: 10/2026

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

AmeriHealth Caritas Pennsylvania Community HealthChoices has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas Pennsylvania Community HealthChoices' clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of "medically necessary," and the specific facts of the particular situation are considered by AmeriHealth Caritas Pennsylvania Community HealthChoices on a case by case basis, when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas Pennsylvania Community HealthChoices' clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas Pennsylvania Community HealthChoices' clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas Pennsylvania Community HealthChoices will update its clinical policies as necessary. AmeriHealth Caritas Pennsylvania Community HealthChoices' clinical policies are not guarantees of payment.

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.

Ananda R, Roslan MHB, Wong LL, Botross NP, Ngim CF, Mariapun J. Efficacy and safety of vagus nerve stimulation in stroke rehabilitation: A systematic review and meta-analysis. *Cerebrovasc Dis*. 2022;1-12. Doi: 10.1159/000526470.

Dawson J, Engineer ND, Cramer SC, et al. Vagus nerve stimulation paired with rehabilitation for upper limb motor impairment and function after chronic ischemic stroke: Subgroup analysis of the randomized, blinded, pivotal, VNS-REHAB device trial. *Neurorehabil Neural Repair*. 2023;37(6):367-373. Doi: 10.1177/15459683221129274.

Dawson J, Engineer ND, Prudente CN, et al. Vagus nerve stimulation paired with upper-limb rehabilitation after stroke: One-year follow-up. *Neurorehabil Neural Repair*. 2020;34(7):609-615. Doi: 10.1177/1545968320924361.

Dawson J, Liu CY, Francisco GE, et al. Vagus nerve stimulation paired with rehabilitation for upper limb motor function after ischaemic stroke (VNS-REHAB): A randomised, blinded, pivotal, device trial. *Lancet*. 2021;397(10284):1545-1553. Doi: 10.1016/s0140-6736(21)00475-x.

Dawson J, Pierce D, Dixit A, et al. Safety, feasibility, and efficacy of vagus nerve stimulation paired with upper-limb rehabilitation after ischemic stroke. *Stroke*. 2016;47(1):143-150. Doi: 10.1161/strokeaha.115.010477.

Department of Veterans Affairs, Department of Defense. Management of stroke rehabilitation clinical practice guideline. https://www.healthquality.va.gov/guidelines/Rehab/stroke/VADoD-2024-Stroke-Rehab-CPG-Full-CPG_final_508.pdf. Published 2024.

Gao Y, Zhu Y, Lu X, et al. Vagus nerve stimulation paired with rehabilitation for motor function, mental health and activities of daily living after stroke: A systematic review and meta-analysis. *J Neurol Neurosurg Psychiatry*. 2023;94(4):257-266. Doi: 10.1136/jnnp-2022-329275.

Kimberley TJ, Pierce D, Prudente CN, et al. Vagus nerve stimulation paired with upper limb rehabilitation after chronic stroke. *Stroke*. 2018;49(11):2789-2792. Doi: 10.1161/strokeaha.118.022279.

Kalagara R, Chennareddy S, Reford E, et al. Complications of implanted vagus nerve stimulation: a systematic review and meta-analysis. *Cerebrovasc Dis*. 2025;54(1):112-120. Doi:10.1159/000536362.

Kwakkel G, Dobkin BH. Vagus nerve stimulation for upper limb function: Significant difference, but clinically important? *Stroke*. 2021;52(10):3407-3409. Doi: 10.1161/strokeaha.121.035648.

Lin DJ, Finklestein SP, Cramer SC. New directions in treatments targeting stroke recovery. *Stroke*. 2018;49(12):3107-3114. Doi: 10.1161/strokeaha.118.021359.

Liu CY, Russin J, Adelson DP, et al. Vagus nerve stimulation paired with rehabilitation for stroke: Implantation experience from the VNS-REHAB trial. *J Clin Neurosci*. 2022;105:122-128. Doi: 10.1016/j.jocn.2022.09.013.(a)

Liu Y, Zhang L, Zhang X, Ma J, Jia G. Effect of combined vagus nerve stimulation on recovery of upper extremity function in patients with stroke: A systematic review and meta-analysis. *J Stroke Cerebrovasc Dis*. 2022;31(6):106390. Doi: 10.1016/j.jstrokecerebrovasdis.2022.106390.(b)

National Institute of Neurological Disorders and Stroke. Post-stroke rehabilitation fact sheet. <https://www.ninds.nih.gov/Disorders/Patient-Caregiver-Education/Fact-Sheets/Post-Stroke-Rehabilitation-Fact-Sheet>. Last reviewed March 08, 2023.

Ramos-Castaneda JA, Barreto-Cortes CF, Losada-Florian D, Sanabria-Barrera SM, Silva-Sieger FA, Garcia RG. Efficacy and safety of vagus nerve stimulation on upper limb motor recovery after stroke. A systematic review and meta-analysis. *Front Neurol*. 2022;13:889953. Doi: 10.3389/fneur.2022.889953.

Tsao CW, Aday AW, Almarzooq ZI, et al. Heart disease and stroke statistics — 2022 update: A report from the American Heart Association. *Circulation*. 2022;145(8):e153–e639.

U.S. Food and Drug Administration. Premarket Approval (PMA) database searched using product code QPY. <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm>. Searched April 29, 2025.

U.S. Food and Drug Administration. MicroTransponder® Vivistim® Paired VNS™ System. Premarket approval letter. P210007. https://www.accessdata.fda.gov/cdrh_docs/pdf21/P210007A.pdf. Dated August 27, 2021.

Wang X, Ding Q, Li T, et al. Application of vagus nerve stimulation on the rehabilitation of upper limb dysfunction after stroke: A systematic review and meta-analysis. *Front Neurol*. 2023;14:1189034. Doi: 10.3389/fneur.2023.1189034.

Winstein CJ, Stein J, Arena R, et al. Guidelines for adult stroke rehabilitation and recovery: A guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke*. 2016;47(6):e98-e169. Doi: 10.1161/str.0000000000000098.

Xie YL, Wang S, Wu Q, Chen X. Vagus nerve stimulation for upper limb motor impairment after ischemic stroke: A meta-analysis. *Medicine (Baltimore)*. 2021;100(46):e27871. Doi: 10.1097/md.00000000000027871.

Zhao K, Yang J, Huang J, Zhao Z, Qu Y. Effect of vagus nerve stimulation paired with rehabilitation for upper limb function improvement after stroke: A systematic review and meta-analysis of randomized controlled trials. *Int J Rehabil Res*. 2022;45(2):99-108. Doi: 10.1097/mrr.0000000000000509.

Policy updates

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

6/2023: Policy references updated.

6/2024: Policy references updated.

6/2025: Policy references updated.