Medical Coverage Policy

Effective Date.....2/15/2026
Next Review Date.....12/15/2026
Coverage Policy Number..... 0350

Vagus Nerve Stimulation (VNS)

Table of Contents

Related Coverage Resources

Deep Brain, and Motor Cortex and Responsive Cortical Stimulation
Electrical Stimulation Therapy and Home Devices
Transcranial Magnetic Stimulation

INSTRUCTIONS FOR USE

The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers

must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses use of an implantable vagus nerve stimulator (VNS) for the treatment of medically intractable seizures and other indications.

Coverage Policy

Vagus nerve stimulation (VNS) with an implantable vagus nerve stimulator is considered medically necessary for the treatment of medically intractable seizures when there is failure, contraindication or intolerance to all suitable medical and pharmacological management.

VNS with an implantable vagus nerve stimulator is considered not medically necessary for any other indication, including but not limited to:

- treatment resistant depression, both unipolar and bipolar
- as an adjunct to rehabilitation therapy for chronic ischemic stroke
- autoimmune disorders (e.g., rheumatoid arthritis)

Coding Information

Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare and Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	**Description**
61886	Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to 2 or more electrode arrays
64553	Percutaneous implantation of neurostimulator electrode array; cranial nerve
64568	Open implantation of cranial nerve (eg, vagus nerve) neurostimulator electrode array and pulse generator
0908T	Open implantation of integrated neurostimulation system, vagus nerve, including analysis and programming, when performed

HCPCS Codes	**Description**
C1767	Generator, neurostimulator (implantable), non-rechargeable

HCPCS Codes	Description
C1778	Lead, neurostimulator (implantable)
C1816	Receiver and/or transmitter, neurostimulator (implantable)
C1820	Generator, neurostimulator (implantable), with rechargeable battery and charging system
C1883	Adapter/Extension, pacing lead or neurostimulator lead (implantable)
L8679	Implantable neurostimulator, pulse generator, any type
L8680	Implantable neurostimulator electrode, each
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, non-rechargeable, includes extension
L8687	Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
L8688	Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension

Considered Not Medically Necessary when used to report an implantable vagus nerve stimulator for any other indication:

CPT®* Codes	Description
61886	Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to 2 or more electrode arrays
64553	Percutaneous implantation of neurostimulator electrode array; cranial nerve
64568	Open implantation of cranial nerve (eg, vagus nerve) neurostimulator electrode array and pulse generator
0908T	Open implantation of integrated neurostimulation system, vagus nerve, including analysis and programming, when performed

HCPCS Codes	Description
C1607	Neurostimulator, integrated (implantable), rechargeable with all implantable and external components including charging system
C1767	Generator, neurostimulator (implantable), non-rechargeable
C1778	Lead, neurostimulator (implantable)
C1816	Receiver and/or transmitter, neurostimulator (implantable)
C1820	Generator, neurostimulator (implantable), with rechargeable battery and charging system
C1883	Adapter/Extension, pacing lead or neurostimulator lead (implantable)
L8679	Implantable neurostimulator, pulse generator, any type
L8680	Implantable neurostimulator electrode, each
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

HCPCS Codes	Description
L8686	Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension
L8687	Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
L8688	Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension

General Background

The vagus nerve is the longest cranial nerve and transmits signals between the brain and multiple organs, including the heart, lungs, digestive system, and sensory pathways from the ear and upper body. An implantable vagus nerve stimulator (VNS) is surgically placed in the chest with a lead wrapped around the left vagus nerve to deliver controlled electrical pulses that modulate brain activity involved in seizures, mood regulation, and inflammatory responses. VNS was first used to reduce the frequency and severity of refractory seizures and has been proposed for use in numerous other indications including treatment-resistant depression, adjunctive stroke rehabilitation, and neuromodulation of autoimmune disorders like rheumatoid arthritis. It is recommended that the implantation procedure be performed by a licensed, trained, and experienced neurosurgeon, general surgeon, vascular surgeon, or an ear-nose-throat surgeon. Contraindications include prior vagotomy and exposure to therapeutic diathermy due to risks of cardiac dysrhythmias or thermal injury to surrounding tissues. Common adverse effects include hoarseness, voice changes, cough, tingling, and shortness of breath, while rare complications include vocal cord paralysis, infection, left facial nerve paralysis, and Horner syndrome (Mandalaneni & Rayi, 2023).

Seizures

A seizure is defined as a shortchange in normal brain activity and can be classified into two groups: generalized or focal. Generalized seizures affect both sides of the brain and can manifest as rapid blinking or staring into space (i.e., absence seizure), or crying out, loss of consciousness, falling, and/or muscle jerks or spasms (i.e., Tonic-clonic seizure). Focal seizures, also known as partial seizures, are localized to one area of the brain and can cause twitching or a change in taste or smell (i.e., simple focal seizure); confusion or inability to respond (i.e., complex focal seizure); or can start as a focal seizure originating in one part of the brain but then spread to a generalized seizure (i.e., secondary generalized seizure). When two or more seizures have occurred, epilepsy is diagnosed. Epilepsy can be caused by stroke, brain tumor, traumatic brain injury, or a central nervous system infection; however, many times the cause is unknown. Pharmacotherapy is a first line treatment for epilepsy and is effective in two out of three people. Surgery may be utilized for focal seizures in an effort to remove the part of the brain that is causing the seizure focus. This is most commonly utilized when the focus is located in the temporal lobe of the brain (Centers for Disease Control and Prevention, 2020).

Epilepsy affects up to five million new individuals annually, with a global prevalence of approximately 50 million. About one-third of people with epilepsy experience drug-resistant epilepsy (DRE), also referred to as intractable or pharmacoresistant epilepsy, where seizures persist despite treatment with anti-seizure medications (ASMs). The primary goal of epilepsy management is to reduce seizure frequency, and ASMs remain the most widely used therapeutic approach. However, individuals with DRE do not respond adequately to these medications. Management of DRE may involve both invasive and non-invasive approaches. Surgical procedures

such as hemispherectomy, temporal lobectomy, and corpus callosotomy are sometimes recommended, but they are highly invasive and carry risks of complications and postoperative deficits. In response to these challenges, neurostimulation techniques have emerged as less invasive alternatives. The U.S. Food and Drug Administration (FDA) has approved three therapies: vagus nerve stimulation (VNS), deep brain stimulation of the anterior nucleus of the thalamus (ANT-DBS), and responsive neurostimulation (RNS). Among these, VNS is a recognized neuromodulation treatment for DRE and is recommended for individuals who are not candidates for surgery or pharmacotherapy (Muniyandi, et al., 2025).

U.S. Food and Drug Administration (FDA)
An implanted vagus nerve stimulator for epilepsy is considered a Class III device and is regulated by the FDA via the Premarket approval (PMA) process. The device is indicated as an adjunctive treatment to reduce the frequency of seizures in individuals aged 4 years and older (S207, 06/23/2017) who have medically refractory partial-onset seizures and have not responded adequately to antiepileptic medications (FDA, 2025).

Device or Product	Identifier	Manufacturer
VNS Therapy® System	P970003	LivaNova, USA, Inc.

*FDA product codes: LYJ

Note: Coverage decisions are not based solely on FDA approval. Device or product names are provided for example purposes only. Their inclusion does not indicate endorsement or preference for any specific brand or model. This list is not intended to reflect all available products or technologies.

Literature Review
Evidence in the peer-reviewed scientific literature indicates that VNS may be a viable option for reducing seizure severity and duration in individuals who remain refractory despite optimal drug therapy or surgical intervention, as well as in those experiencing debilitating side effects from antiepileptic medications. After VNS implantation seizure frequency is usually reduced by 50%, which is similar to the result of many drugs but without the side effects. Most individuals are not seizure-free after treatment with VNS. More recent studies have investigated the efficacy of VNS as an adjunct therapy for individuals with generalized seizures and for the pediatric population. Evidence suggests that VNS may offer significant health benefits for those experiencing generalized seizures and children with refractory epilepsy (Muniyandi, et al., 2025; Suller, et al., 2025; Feygina, et al., 2023; Panebianco, et al., 2022; Dibué, et al., 2021; Dibué-Adjei, et al., 2019; Ryvlin, et al., 2014).

Professional Societies/Organizations
The **American Academy of Neurology (AAN)** guideline on vagus nerve stimulation (VNS) for epilepsy states VNS may be considered for seizures in children, for Lennox-Gastaut syndrome (LGS)-associated seizures, and for improving mood in adults with epilepsy. VNS may be considered to have improved efficacy over time. Children should be carefully monitored for site infection after VNS implantation (Level C). Level C is defined as possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. The authors recommendations for further research state that more information is needed on the treatment of primary generalized epilepsy in adults and that parameter settings (e.g., cycle time length) would potentially help with better VNS management and use. Techniques to reduce infection risk at the VNS site in children should be developed and further information is needed on the effects of VNS on sleep apnea (Morris, et al., 2013; reaffirmed 2025).

Treatment Resistant Depression

Treatment resistant depression (TRD) is a clinical condition characterized by inadequate response to four or more antidepressant treatments administered at adequate dose and duration with confirmed adherence. It affects approximately 30% of individuals with major depressive disorder (MDD). Risk factors for TRD include older age, lower socioeconomic status, childhood trauma, greater baseline severity, longer illness duration, psychotic features, anxiety symptoms, and comorbid physical and psychiatric conditions. Detection of TRD requires ruling out pseudo-resistance, which may result from misdiagnosis (e.g., bipolar disorder), inadequate treatment trials, poor treatment adherence, or pharmacokinetic variability. Management strategies for TRD include extending or switching antidepressant trials, combining antidepressants, and using adjunctive treatments such as psychotherapeutic interventions (e.g., cognitive behavioral therapy (CBT), interpersonal psychotherapy) and/or neurostimulation treatments such as electroconvulsive therapy (ECT), repetitive transcranial magnetic stimulation (rTMS), or vagus nerve stimulation (VNS) (McIntyre, 2023).

U.S. Food and Drug Administration (FDA)

An implanted autonomic nerve stimulator for the treatment of depression is classified by the FDA as a Class III medical device and is regulated under the Premarket Approval (PMA) pathway. The device is indicated for the adjunctive treatment of chronic or recurrent depression (S050, 07/15/2005) for adults experiencing a major depressive episode that have not achieved an adequate response to four or more antidepressant treatments (FDA, 2025).

Device or Product	Identifier	Manufacturer
VNS Therapy® System	P970003	LivaNova, USA, Inc.

*FDA product codes: MUZ

Note: Coverage decisions are not based solely on FDA approval. Device or product names are provided for example purposes only. Their inclusion does not indicate endorsement or preference for any specific brand or model. This list is not intended to reflect all available products or technologies.

Literature Review

Over the last twenty years the safety and efficacy of vagus nerve stimulation (VNS) for the management of treatment resistant depression (TRD) has been evaluated in technology assessments, open-label, observational studies, randomized controlled trials (RCTs) (n=30–795 individuals), and systematic reviews with meta-analyses (n=22 studies), with follow up ranging from 10 weeks to 5 years. These studies have compared VNS to sham stimulation, treatment as usual (TAU), and pharmacologic interventions, and have reported mixed results. In most studies there is a lack of clinically significant (i.e., ≥ 50% reduction in symptoms sustained at ≥40%) improvement in depressive symptoms between VNS and sham or TAU, however, there have been reports of significant improvements in quality of life and suicidality in individuals treated with VNS. Meta-analyses have shown that VNS is generally safe and well-tolerated, with common side effects including voice hoarseness, neck pain, and sore throat. However, serious adverse events including cardiac complications or the emergence of manic symptoms have been reported. In general, studies have been limited by lack of control or placebo groups, lack of randomization, and high attrition rates. Additionally, there is a lack of consensus on optimal stimulation parameters, dosing considerations, and mechanism (Austelle, et al., 2021; McAllister-Williams et al., 2020; Kumar et al., 2019; Aaronson, et al., 2017; Conway, et al., 2018).

As part of an ongoing leg of the RECOVER clinical trial, Conway et al. (2024) conducted a randomized, multicenter (n=84), double-blind, sham-controlled trial to evaluate adjunctive vagus nerve stimulation (VNS) in individuals with marked treatment-resistant depression. Adults

(n=493) diagnosed with major depressive disorder (MDD) with ≥4 failed adequate antidepressant treatments in the current major depressive episode (MDE) were randomized into two groups: VNS + treatment as usual (TAU) (n=249) or sham VNS + TAU (n=244). During the randomized and blinded phase participants could not start an acute course of electroconvulsive therapy (ECT), and during the 12-month study period physicians were encouraged not to change baseline antidepressants or other psychotropic medications. Exclusion criteria were substance use disorder, severe personality disorder, history of psychotic symptoms or a suicide attempt within 6 months, or a primary diagnosis of obsessive-compulsive disorder, eating disorder, post-traumatic stress disorder, dementia, or major neurocognitive disorder. The primary outcome measure was defined as patients achieving a ≥ 50% reduction from baseline in Montgomery-Åsberg Depression Rating Scale (MADRS) response. Secondary outcomes were measured using Clinical Global Inventory–Impression (CGI-I), Quick Inventory of Depressive Symptomology–Self Report (QIDS-SR) and Quick Inventory of Depressive Symptomology–Clinician (QIDS-C) scores. Assessments were completed at baseline and in months 3 through 12. After the end of the 12-month randomized clinical trial phase, participants consented to a 4-year blinded observation period that is ongoing as of this publication. To date there are no significant differences in the primary outcome of percent time in MADRS response between active from sham VNS. Regarding secondary measures, active VNS demonstrated significantly more percent time in response on the CGI-I (p=0.004) and QIDS-SR (p=0.049). In known adverse events, active VNS exceeded sham VNS in rate of dyspnea (p=0.035). The authors noted limitations in participant selection, heterogeneity in stimulation parameters, blinding, use of telephone follow-up, and participant attrition.

Over the same double-blind, 12-month observation period of the above-mentioned leg of the RECOVER trial, Rush et al. (2024) evaluated the effects of adjunctive versus sham vagus nerve stimulation (VNS) on quality of life (QoL) and function. QoL outcome measures were reported using scores from the Quality-of-Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q), Mini-Q-LES-Q, and EuroQoL Five-Dimension Questionnaire (EQ-5D-5L). Additionally, function measures were reported via the World Health Organization Disability Assessment Schedule (WHODAS) 2.0 and Work Productivity and Activity Impairment Questionnaire (WPAI). Active VNS showed significant change in baseline scores in the Mini-Q-LES-Q (p=0.050) and WPAI item 6 (health condition's effect on regular activities [p=0.050]). Time spent in clinically meaningful benefit was also significant per Q-LES-Q (p=0.029), Mini-Q-LES-Q (p=0.011), and WPAI item 6 (p=0.039). There were no significant differences in The WHODAS 2.0 (p=0.304) and EQ-5D visual analog scale (p=0.125). Author noted limitations include use of self-reported questionnaires, and limitations with blinding. An additional limitation is short-term follow-up.

McAllister-Williams et al. (2020) completed a prospective, multicenter, open-label registry study involving 156 adults (mean age 47 years) to examine illness characteristics, treatment history, response durability, and suicidality over a five-year period in individuals with treatment resistant bipolar depression (TRBD). Participants were included if they were experiencing an active major depressive episode lasting two years or longer (either unipolar or bipolar) or had a history of at least three major depressive episodes, including the current one, along with inadequate response to four or more adequate antidepressant treatments. Individuals with a history of psychotic disorders, rapid-cycling bipolar disorder, or psychotic features in the current episode were excluded. Participants chose between receiving vagus nerve stimulation plus treatment as usual (VNS + TAU; n=97) or treatment as usual alone (TAU; n=59). The VNS + TAU group had a significantly higher proportion of individuals with bipolar I disorder and fewer with bipolar II compared to the TAU group (p=0.0158). At baseline, the VNS + TAU group also had more depressive episodes, psychiatric hospitalizations, lifetime suicide attempts, higher suicidality scores, more severe symptoms, and greater prior use of electroconvulsive therapy. Lifetime medication use was similar between groups. The primary outcome was defined as a ≥ 50% reduction from baseline in the Montgomery–Åsberg Depression Rating Scale (MADRS) total score, while maintenance of response was defined as a MADRS score remaining ≥ 40% below baseline.

Time-to-event outcomes were analyzed using Kaplan–Meier methods and compared via log-rank tests. Suicidality was assessed using MADRS Item 10, and additional psychiatric outcomes were measured using the Quick Inventory of Depressive Symptomatology–Self Report (QIDS-SR) and the Clinical Global Impression (CGI) scale. Follow-up occurred routinely between 3 months and 5 years. Results showed that 63% of participants in the VNS + TAU group achieved an initial response (≥ 50% MADRS reduction) compared to 39% in the TAU group, with significantly faster time-to-response in the VNS + TAU group ($p<0.03$). Maintenance of response during the first year was 75.4% in the VNS + TAU group and 82.6% in the TAU group. The Kaplan–Meier estimate of median time-to-relapse was not statistically significant between groups. The mean reduction in suicidality score across study visits was significantly greater in the VNS + TAU group ($p<0.001$). Limitations of the study include lack of randomization, heterogeneity in severity of illness, uncontrolled VNS stimulation parameters, and a high attrition rate.

In 2019, Bottomley, et al. conducted a systematic review of randomized controlled trials, non-randomized comparative studies, single-arm studies, and case series to compare treatment as usual (TAU) for treatment resistant depression (TRD) to vagus nerve stimulation (VNS) used as an adjunct to TAU. There were a total of 1,580 participants with individual sample sizes ranging from 5–795 participants. Studies (n=22) were included if they evaluated VNS as an adjunct to TAU or TAU alone and included an adult population diagnosed with TRD. The intervention was VNS used as an adjunct to TAU. Comparators included: sham, various stimulation levels, and TAU only. The primary outcomes included efficacy defined as patients achieving a ≥ 50% reduction from baseline in a depression rating scale and remission defined as maintenance of the reduction from baseline on a depression rating scale (e.g., Montgomery Asberg Depression Rating Scale (MADRS), Hamilton Rating Scale for Depression (HAMD)). Secondary outcome measures included: adverse events, hospitalizations, serious adverse events, suicide, all-cause mortality, mania, dropouts, and discontinuation of VNS. Follow-up ranged from three to over six years. The percent of individuals who underwent VNS plus TAU and achieved a ≥ 50% reduction from baseline on the MADRS scale was 23.9%, 38.9%, and 52.6% at six, 12, and 24 months, respectively. The percent of individuals who underwent TAU only and achieved a ≥ 50% reduction from baseline on the MADRS scale was 13.8%, 17.5%, and 18.5% at six, 12, and 24 months, respectively. For those studies using the HAMD scale, the percent of individuals achieving a ≥ 50% reduction from baseline was 29.9%, 43.4%, and 36.7% at six, 12, and 24 months. The pooled TAU only HAMD responder rate was only available at 12 months and was 9.6%. The pooled rate of serious adverse events in patients who underwent VNS plus TAU was 5.5% at 12 months. No serious adverse event data was available for those who underwent VNS plus TAU at six months or for those who underwent TAU only at any time point. The all-cause mortality rate for those who underwent VNS plus TAU at three, 12, and 24 months was 0.0%, 0.4%, and 1.4%, respectively. For those who underwent TAU only, the pooled mortality rate at three, six, 12, and 24 months was 0.3%, 0.3%, 0.3%, and 0.7%, respectively. Author noted limitations of the review included: the lack of randomized controlled trials and heterogeneity of treatment protocols, study designs, follow-up, and severity of illness definitions. Additional, high quality and long-term reviews are needed to assess the safety and efficacy of VNS for the treatment of treatment resistant depression.

Aaronson et al. (2017) reported long-term outcomes from the five-year post-marketing surveillance study of individuals with treatment resistance depression treated with VNS or "treatment as usual." The prospective, open-label, nonrandomized, observational registry study was conducted at 61 U.S. sites. The study included a total of 795 patients who were experiencing a major depressive episode (unipolar or bipolar depression) of at least two years' duration or had three or more depressive episodes (including the current episode), and who had failed four or more depression treatments (including ECT). Patients with a history of psychosis or rapid-cycling bipolar disorder were excluded. The primary efficacy measure was response rate, defined as a decrease of ≥50% in baseline Montgomery Åsberg Depression Rating Scale (MADRS) score at any post baseline visit during the five-year study. Secondary efficacy measures included remission.

Patients had chronic moderate to severe depression at baseline (the mean MADRS score was 29.3 [SD=6.9] for the treatment-as-usual group and 33.1 [SD=7.0] for the adjunctive VNS group). The registry results indicate that the adjunctive VNS group had better clinical outcomes than the treatment- as-usual group, including a significantly higher five-year cumulative response rate (67.6% compared with 40.9%) and a significantly higher remission rate (cumulative first-time remitters, 43.3% compared with 25.7%). A sub-analysis demonstrated that among patients with a history of response to ECT, those in the adjunctive VNS group had a significantly higher five-year cumulative response rate than those in the treatment-as-usual group (71.3% compared with 56.9%). A similar significant response differential was observed among ECT non-responders (59.6% compared with 34.1%). The naturalistic, observational study design did not allow for random assignment of participants to treatment groups; thus, participants were not blinded to treatment. A significant number of participants in both groups withdrew early from the study. Of the 358 patients (45%) who withdrew early, 195 were from the VNS arm (40%) and 163 were from the treatment-as-usual arm (54%). The reasons for early withdrawal were similar between the treatment arms. The significantly higher treatment response rate observed in the VNS arm may represent a placebo effect, as participants with an implanted device may have had a higher expectation of therapeutic improvement.

Professional Societies/Organizations
The **American Psychological Association (APA)** clinical practice guideline addressing the treatment of depressive disorders in children, adolescents, adults and older adults (2019) examined the efficacy of psychological treatments, pharmacotherapy and complementary and alternative medicine treatments. VNS was not listed as a treatment modality within the practice guideline.

The **American Psychiatric Association (APA)** practice guideline for the treatment of patients with major depressive disorder states that electroconvulsive therapy (ECT) remains the treatment of best established efficacy against which other stimulation treatments (e.g., VNS, deep brain stimulation, transcranial magnetic stimulation, other electromagnetic stimulation therapies) should be compared. VNS may be an additional option for individuals who have not responded to at least four adequate trials of antidepressant treatment, including ECT [III]. For patients~~,~~ whose depressive episodes have not previously responded to acute or continuation treatment with medications or a depression focused psychotherapy but who have shown a response to ECT, maintenance ECT may be considered [III]. Maintenance treatment with VNS is also appropriate for individuals whose symptoms have responded to this treatment modality [III]. According to the APA, relative to other antidepressive treatments, the role of VNS remains a subject of debate. However, it could be considered as an option for patients with substantial symptoms that have not responded to repeated trials of antidepressant treatment. The three APA rating categories represent varying levels of clinical confidence:

- I: Recommended with substantial clinical confidence
- II: Recommended with moderate clinical confidence
- III: May be recommended on the basis of individual circumstances (Gelenberg, et al., 2010).

The 2022 **Department of Veterans Affairs and the Department of Defense** evidence-based clinical practice guideline for the management of major depressive disorder recommends against offering vagus nerve stimulation (VNS) for patients with major depressive disorder, including patients with severe treatment resistant depression outside of a research setting. They stated that there is no evidence showing a difference between VNS and sham placebo. The guideline notes that the potential harms and burdens outweigh the benefits.

There is insufficient evidence in the published peer-reviewed medical literature to assess the safety, efficacy, and long-term outcomes of an implantable vagus nerve stimulator for managing treatment-resistant depression.

Stroke Rehabilitation

Ischemic cerebrovascular disease is caused by a reduction in blood supply to the brain, leading to cell death in the brain, spinal cord, or retina. It accounts for approximately 85% of all strokes and may result from atherosclerosis, cardiogenic embolism, or small-vessel disease. The pathophysiology involves occlusion of cerebral arteries, which may be focal, multifocal, or global, and can be due to thrombotic or embolic events. Risk factors include hypertension, diabetes mellitus, atrial fibrillation, carotid artery stenosis, smoking, physical inactivity, and sickle cell disease. Clinical symptoms vary depending on the vascular territory affected and may include hemiparesis (i.e., weakness or partial paralysis on one side of the body), sensory deficits, aphasia, visual field defects, and coordination problems. Rehabilitation treatment is multidisciplinary involving speech therapy, physical therapy, and occupational therapy. Vagus nerve stimulation paired with standard rehabilitation has emerged as a potential therapy for improving upper limb motor function after ischemic stroke (Goldstein, 2024).

Chronic stroke (i.e., >6 months) remains a leading cause of long-term disability in the United States, often resulting in persistent deficits in upper extremity motor function that significantly impair activities of daily living. Recovery of fine motor skills typically requires intensive rehabilitation aimed at promoting neuroplasticity, the brain's ability to reorganize and strengthen residual neural networks to restore function. Recent clinical studies have explored the neuromodulatory effects of vagus nerve stimulation (VNS) in enhancing neuroplasticity. When paired repeatedly with motor or sensory tasks, VNS is proposed to increase the number of active cortical neurons during the paired activity, thereby facilitating reorganization of motor networks and improving synaptic efficacy (Khan, et al., 2025).

U.S. Food and Drug Administration (FDA)

A vagus nerve stimulation device used for stroke rehabilitation is FDA-regulated through the Premarket Approval (PMA) process as a Class III medical device. The indication for use is in individuals with chronic ischemic stroke with moderate to severe upper extremity motor deficits. It is intended to be used as an adjunct to rehabilitation therapy to reduce motor impairment and improve arm function. The device is contraindicated in individuals with a history of bilateral or left cervical vagotomy (FDA, 2025).

Device or Product	Identifier	Manufacturer
MicroTransponder® Vivistim® Paired VNS System	P210007	MicroTransponder Inc.

*FDA product codes: QPY

Note: Coverage decisions are not based solely on FDA approval. Device or product names are provided for example purposes only. Their inclusion does not indicate endorsement or preference for any specific brand or model. This list is not intended to reflect all available products or technologies.

Literature Review

Khan et al. (2025) completed a systematic review and meta-analysis of eight studies involving 498 adults (aged 18–80 years; 15–106 participants per study) to assess the effectiveness of implanted vagus nerve stimulation (iVNS) paired with rehabilitation therapy in individuals with unilateral supratentorial ischemic stroke and upper extremity deficits. Stroke chronicity ranged from 6 months to 10 years. The intervention group included 245 participants (63.2% male; mean age 59), while the control group had 252 participants (64.4% male; mean age 61). The studies

included RCTs (n=4), quasi-experimental studies, cohort studies, and case-control studies that compared iVNS paired with neurorehabilitation to standard rehabilitation methods, sham stimulation, or no intervention. Excluded studies were case reports, editorials, reviews, letters to the editor, conference abstracts, book chapters, animal and molecular studies, small case series (n<5), and expert opinions lacking clinical data. Primary outcomes were measured using the Fugl-Meyer Assessment for Upper Extremity (FMA-UE) and Wolf Motor Function Test (WMFT) scales. Most studies administered VNS therapy for 6 weeks with follow-up at 90 days; two studies (n=15 each) extended therapy to 1 year and 3 years. Across studies both groups showed post-intervention and follow-up improvements, with pooled analysis revealing a significant improvement in FMA-UE scores in the intervention group (p=0.04). No significant differences were found in WMFT scores between groups. Six studies reported non-serious adverse events (AEs), including transient dysphagia, taste disturbances, post-stimulation nausea, mild hoarseness, and neck stiffness/spasticity. One study reported serious AEs related to implantation surgery, including wound infection requiring IV antibiotics and shortness of breath. No statistically significant differences in AEs were observed between groups. Author noted limitations include limited availability of high-quality studies, heterogeneity in outcome reporting, absence of demographic data, lack of data on vascular territories and posterior circulation strokes limiting generalizability, and potential conflicts of interest in three clinical trials. Additional noted limitations include small sample sizes, short term follow up, and heterogeneity in symptom severity, comorbidities, and stimulation parameters.

Kimberley et al. (2025) conducted an unblinded, partial crossover, pooled 1-year post hoc analysis of data from the fully blinded, sham-controlled VNS-REHAB trial. The study evaluated the long-term effects of vagus nerve stimulation (VNS) paired with upper extremity rehabilitation in individuals with chronic ischemic stroke. The study enrolled 108 participants (aged 22–80 years) across 19 sites, all with a history of unilateral supratentorial ischemic stroke occurring 9 months to 10 years prior to enrollment. Key exclusion criteria included: history of hemorrhagic stroke, ongoing dysphagia or aspiration difficulties, medications interfering with VNS neurotransmitter effects, prior bilateral or unilateral vagus nerve injury, severe depression, poor surgical candidacy, current use of any other stimulation device (e.g., pacemaker, other neurostimulator) or other investigational device, medical or mental instability, pregnancy, diathermy requirement, active rehabilitation or Botox within 4 weeks prior to enrollment, severe spasticity of the upper limb, or significant sensory loss. Participants received 18 sessions of intensive, task-specific rehabilitation (3x/week for 6 weeks) and 3 months of self-directed home exercise, with either active (n=53) or sham (n=55) VNS. After the blinded phase, control participants crossed over to active VNS. All participants continued self-initiated VNS therapy for one year. Outcome measures were assessed using the Fugl-Meyer Assessment UE (FMA-UE), Wolf Motor Function Test (WMFT), and patient reported outcomes including Motor Activity Log (Quality of Movement and Amount of Use), Stroke Impact Scale (Activities of Daily Living and Hand), EQ-5D, and Stroke-Specific Quality of Life. At 1-year follow-up, 74 participants (69%) completed the observation phase and showed significant improvements across all measures (p<0.001; EQ-5D p<0.05). Four serious adverse events (dyspnea, infection, acute infarct) occurred post-blinded phase and were deemed unrelated to the intervention (3 in VNS group, 1 in control). Study limitations included participant attrition, unblinding, incomplete data reporting, lack of diversity metrics, unmonitored home exercise adherence, small sample size, and short follow-up duration.

Dawson, et al. (2021) conducted a pivotal, triple-blinded, randomized controlled trial (RCT) (n=108) to evaluate the safety and efficacy of vagus nerve stimulation (VNS) paired with rehabilitation on improving arm function after stroke. Participants ranged in age from 22–80 years. Sixty-four percent of participants in the VNS group were male, 79% were white, 17% were African American, and 2% were Asian, Indian, or other. Sixty-five percent of participants in the control group were male, 78% were white, 16% were African American, and 7% were Asian, Indian, or other. Patients were included in the study if they had a history of supratentorial

ischemic stroke having occurred between nine months and ten years prior to enrollment and had severe arm impairment defined as a Fugl-Meyer Assessment-Upper Extremity (FMA-UE) score of 20–50 points. All patients were implanted with the Vivistim System VNS device and received six weeks of in-clinic therapy three times per week for six weeks followed by a home exercise program. The intervention consisted of active VNS (i.e., 0.8mA, 100ms, and 30Hz) used in conjunction with stroke rehabilitation timed so that stimulation occurred with each repetition of movement (VNS group) (n=53). The comparator was sham VNS (i.e., 0 MA) paired with stroke rehabilitation (control group) (n=55). Participants in both treatment groups received five active stimulations in reducing strengths at the start of each therapy session in an effort to reduce the participant's ability to infer treatment allocation. In-clinic rehabilitation consisted of high-repetition, task-based, functional, individualized, and progressive upper limb exercises. The change in impairment measured by the FMA-UE score on the first day after completion of in-clinic therapy was the primary outcome measured. The secondary outcome measured was the FMA-UE score at 90 days after completion of in-clinic therapy. Baseline assessments occurred at one week after device implantation. Follow-up occurred at 30 and 90 days after the completion of in-clinic therapy. Compared to baseline, FMA-UE scores were significantly improved in the VNS group compared to the control group at the first day after completion of in-clinic therapy (p=0.0014). At 90 day follow-up, FMA-UE scores remained significantly improved in the VNS group compared to the control group (p=0.0077). Forty percent of participants in the VNS group and 55% of participants in the control group experienced an adverse event deemed "possibly, probably, or definitely" related to device implantation and were mostly due to post-op pain. Twenty-five percent of participants in the VNS group and 16% of participants in the control group experienced an adverse event deemed either "possibly, probably, or definitely" related to device use. Vocal cord paralysis related to surgery occurred in one patient in the control group and resolved after five weeks. There were no significant between-group differences of adverse event reports. Author noted limitations of the study included the fact that results cannot be generalized to individuals who did not meet inclusion criteria or who had experienced different types of stroke or other neurological disorders. The authors also pointed to their small sample size, short-term follow-up, and disproportionate number of male participants as limitations. Additional high quality studies with long-term follow-up and larger and more diverse patient populations are needed to fully evaluate the safety and efficacy of VNS for improving upper extremity function in individuals with stroke.

Professional Societies/Organizations
The **American Heart Association (AHA)/American Stroke Association (ASA)** clinical practice guideline, affirmed by the **American Academy of Neurology (AAN)**, addressed adult stroke rehabilitation and evaluated the efficacy of various post-stroke treatments for mobility. VNS was not included as a treatment modality within the guideline (Winstein, et al., 2016).

The 2024 **Department of Veterans Affairs and the Department of Defense** evidence-based clinical practice guideline for the management of stroke rehabilitation states there is insufficient evidence to recommend for or against vagus nerve stimulation (VNS) as an adjunct therapy for acute or chronic motor deficits post-stroke. The guideline highlights risks associated with surgically implanted VNS devices, including vocal cord paresis, dysphagia, hoarseness, shortness of breath, infection, bleeding, and cardiac arrhythmia. It also notes contraindications such as arrhythmia and sleep apnea, both of which are common in the stroke population, would eliminate eligibility for many individuals. They indicate the available evidence is considered low quality, based on a small number of randomized controlled trials with limited sample sizes and concerns about bias. The guideline notes the potential harms slightly outweighed the benefits of VNS considering the risks of surgery and post-operative adverse effects.

Clinical validation of invasive VNS remains limited, with heterogeneous treatment responses driven by variability in stroke subtype, lesion location, patient characteristics, and

non-standardized stimulation parameters. Large, multicenter trials using biomarker-guided stratification, standardized stimulation protocols, and long-term functional and quality-of-life follow-up are needed to clarify optimal dosing strategies, assess durability of benefit, and support broader clinical implementation (Wang, et al., 2025) The current available evidence is insufficient to permit conclusions regarding the efficacy and safety of implantable VNS as an adjunct therapy in chronic stroke rehabilitation.

Autoimmune Disorders

Autoimmune disorders arise from dysregulated immune activity in which the body mounts an inflammatory response against its own tissues. This chronic inflammation can result in persistent pain, tissue injury, and long-term functional impairment. Although the exact etiology is not fully understood, contributing factors include environmental exposures and, in some conditions, genetic susceptibility. Clinical manifestations vary by disease and may include inflammatory joint symptoms (e.g., rheumatoid arthritis), gastrointestinal disturbances (e.g., Crohn's disease, ulcerative colitis), and multisystem features such as fatigue, musculoskeletal pain, and dry eyes or dry mouth (e.g., Sjögren's syndrome) (Chan et al., 2025; Lombo et al., 2025).

Management typically involves pharmacologic immunomodulation, including conventional synthetic disease-modifying antirheumatic drugs (DMARDs) such as methotrexate; biologic agents targeting cytokine and co-stimulatory pathways (e.g., TNF-α inhibitors, IL-6 inhibitors, CTLA-4–Ig, B-cell therapies); targeted synthetic DMARDs such as JAK inhibitors; and glucocorticoids. However, first line treatments have significant side effects including increased risk for infection, diabetes, mood disorders, osteoporosis, and cardiac events (Lombo et al., 2025; Tesser et al., 2025). Despite multiple therapeutic options, inadequate or lost response remains common: approximately 40% of patients with rheumatoid arthritis fail at least one DMARD, and multidrug resistance occurs in a subset. In Crohn's disease, 30–50% of patients fail or lose response to anti-TNF therapy (Lombo et al., 2025).

Neuroimmune modulation using vagus nerve stimulation (VNS) has emerged as a potential adjunctive treatment strategy aimed at regulating inflammatory activity by influencing how the nervous and immune systems communicate. VNS is believed to activate the "inflammatory reflex," thereby decreasing production of key pro-inflammatory cytokines such as tumor necrosis factor (TNF), interleukin-6 (IL-6), and interleukin-1 beta (IL-1β). Through the cholinergic anti-inflammatory pathway, vagal signaling modulates immune cell activity and suppresses cytokine release, potentially improving symptoms across autoimmune conditions. Clinical studies have explored the use of VNS in treatment of disorders such as rheumatoid arthritis, Crohn's disease, psoriatic arthritis, ankylosing spondylitis, and systemic lupus erythematosus as a means to reduce inflammatory biomarkers (e.g., IL-6), improve clinical symptoms, and support disease remission in some individuals (Chan et al., 2025; Lombo et al., 2025).

U.S. Food and Drug Administration (FDA)

A vagus nerve stimulator used for rheumatoid arthritis is regulated by the FDA as a Class III medical device under the Premarket Approval (PMA) process. Its approved indication is for adult patients with moderately to severely active rheumatoid arthritis who have had an inadequate response, loss of response, or intolerance to one or more biologic or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) (FDA, 2025). The device is contraindicated in individuals who have undergone a vagotomy or splenectomy (SetPoint Medical, 2025).

Device or Product	Identifier	Manufacturer
SetPoint System	P240039	SetPoint Medical

*FDA product codes: SFJ

Literature Review
Evidence on the safety and efficacy of vagus nerve stimulation (VNS) for autoimmune disorders based on its proposed immunomodulatory effects remains limited. Most available data come from pilot studies, non-randomized trials, case reports, and small case series, with only a few randomized controlled trials. Reported benefits primarily involve reductions in disease activity scores and pro-inflammatory cytokines; however, outcomes vary substantially across studies, reflecting the heterogeneity of autoimmune conditions and the multifaceted mechanisms of VNS. Overall, the evidence base is constrained by small sample sizes (n=1–60), diverse study designs and stimulation parameters, and short follow-up periods, typically 3–12 months (Chan et al., 2025; Liu et al., 2025).

Tesser et al. (2025) conducted RESET RA, a double blind, randomized, sham controlled trial evaluating vagus nerve stimulation (VNS) in adults with moderately to severely active rheumatoid arthritis (RA). A total of 242 participants (aged 22–75 years; mean RA duration 12.4 years) were randomized to active VNS for 3 months (n=122) or sham stimulation for 3 months followed by crossover to open label treatment (n=120). Eligible participants had >4 tender and >4 swollen joints (28 joint count), prior treatment with ≥1 conventional disease modifying antirheumatic drug (csDMARD) (e.g., methotrexate) for ≥12 weeks at a stable dose for ≥4 weeks, and inadequate response or intolerance to ≥1 biologic or targeted synthetic disease modifying antirheumatic drug (b/tsDMARD). Elevated acute phase reactants (e.g. serum C-reactive protein) were not required. Exclusion criteria included prior vagotomy, partial or complete splenectomy, significant cardiovascular disease, and regular nicotine use within the preceding two years. Active VNS consisted of a 1-minute daily pulse train delivered at 10 Hz (mean 1.8 mA; maximum 2.5 mA); the sham group received 0 mA. The primary endpoint was ACR20 response at 3 months, defined as ≥20% improvement in tender and swollen joint counts and ≥3 of 5 additional measures (HAQ DI, patient global assessment, patient pain, evaluator global assessment, and hs CRP). Secondary endpoints included RAMRIS bone erosion progression, EULAR good/moderate response, and DAS28 CRP. At 3 months, the active VNS group achieved a significantly higher ACR20 response (p=0.0209). Secondary outcomes also favored VNS, with improved EULAR good/moderate response (p=0.0048) and higher DAS28 CRP low disease activity/remission rates (p=0.0154). Overall RAMRIS scores were similar between groups; however, among patients with an erosive risk phenotype, erosion progression was reduced with active VNS (p=0.016). Follow-up through 12 months was completed by 96.3% of participants. Across both arms at 12 months, ACR20 response was 57.6%, EULAR good/moderate response was 77.3%, DAS28 CRP low disease activity/remission was 44.8%, and CDAI low disease activity/remission was 43.9%. Nonserious implantation related events occurred in 15.6% of participants, commonly transient vocal cord paresis (4.5%) and dysphonia (2.9%), generally resolving within one year. Additional mild to moderate surgical site events occurred in 5.4% (n=13), including swelling/inflammation (n=6), hypoesthesia (n=2), stitch abscess/infection (n=2), pain (n=1), erythema (n=1), and a suture complication (n=1). Serious procedure related events occurred in 1.7% (n=4) and resolved without sequelae; these included postoperative incision site swelling, transient vocal cord paresis with dysphagia, intraoperative pharyngeal perforation, and postoperative dysphonia. Mild stimulation related discomfort occurred in approximately 4–5% of individuals and was managed by parameter adjustment. Six devices were electively explanted before 12 months due to device malfunction (n=1), chronic incision site pain (n=1), gastrointestinal symptoms attributed to stimulation (n=1), or patient request for removal because of perceived lack of benefit (n=3). Author noted limitations of the study include the 3-month controlled phase. Additional limitations include short follow-up duration and potential conflict of interests.

Lombo et al. (2025) conducted a systematic review of 12 clinical trials (332 total participants; n=5–113 per study) evaluating vagus nerve stimulation (VNS) for autoimmune conditions, including rheumatoid arthritis (RA), Crohn's disease (CD), polymyalgia rheumatica (PMR), psoriatic arthritis (PsA), ankylosing spondylitis (AS), systemic lupus erythematosus (SLE), and

systemic sclerosis (SSc). Eligible studies were open label (n=8) or sham controlled (n=4) and required reporting of peripheral blood inflammatory biomarkers (e.g., CRP, IL 6, IL 1β, IL 10, TNF α, IFN γ) in adults; abstracts and ex vivo inflammatory models were excluded. Both invasive VNS (iVNS) and non invasive VNS (nVNS) were assessed, with iVNS stimulation parameters varying across protocols, including 30 second to 5 minute stimulation periods, frequencies centered around 10 Hz, pulse widths of 250–500 μs, and intensities ranging from 0.10–20 mA depending on titration schedules. Sham comparators consisted of stimulation off devices, zero amplitude stimulations, low frequency sham protocols, or time matched non active transcutaneous stimulation. Primary outcomes focused on changes in pro inflammatory cytokines, while secondary outcomes addressed clinical disease severity. Follow-up durations ranged from 4 days to 12 months. Across iVNS studies in RA, DAS28 CRP improved significantly at 42 days, although CRP reductions were not significant; ACR20 was achieved in 20% and ACR50 in one participant, with no responses in sham. In CD, early pilot data demonstrated normalization of CRP in 67% of patients without statistical testing, universal CDEIS remission, and reductions in digestive pain. Subsequent CD studies showed reductions in CRP and fecal calprotectin (71% and 57% normalized, respectively), stabilization of cytokines (IL 6, TNF α, IL 22, IL 23, IFN γ) in most patients, and significant reductions in fecal calprotectin, though CRP reductions did not reach significance. Additional findings included TNF α (−46%) and IFN γ (−52%) reductions, IL 6 increases, and CDAI remission in 27% of participants. Reported iVNS related adverse events included Horner's syndrome, procedural pain, nausea, and one device removal due to postoperative infection. Limitations included the small number of sham controlled trials, limited blinding, heterogeneity in disease severity and stimulation parameters, variability in dosing schedules, and short follow-up durations. The authors concluded that larger, rigorously designed studies are needed to more confidently establish VNS as a therapeutic option for autoimmune conditions.

Professional Societies/Organizations
The **American College of Gastroenterology (ACG)** clinical guidelines for management of Chron's disease and Ulcerative colitis in adults (2025) do not include any recommendations for use of VNS as a treatment modality for managing these conditions (Lichtenstein, et al., 2025; Rubin, et al., 2025).

The **American College of Rheumatology (ACR)** clinical practice guideline for the treatment of rheumatoid arthritis (2021) addresses the pharmacologic management of rheumatoid arthritis. VNS was not included as a treatment modality within the guideline (Fraenkel, et al., 2021).

The current available evidence is insufficient to permit conclusions regarding the efficacy and safety of implantable VNS as an adjunct therapy in autoimmune disorders. Additional large-scale multicenter studies with standardized stimulation protocols and long-term follow-up are needed.

Other Indications
Vagus nerve stimulation (VNS) has been proposed for use in a wide range of potential indications including, but not limited to: Alzheimer's disease, anxiety related disorders, cancer, chronic heart failure, headaches/migraines, memory and learning impairments, neurodevelopmental disorders, obesity, pain syndromes, posttraumatic stress disorder, and tinnitus. The peer-reviewed scientific literature regarding the use of VNS for these indications has been evaluated in randomized controlled trials, systematic reviews, and observational and feasibility studies. The evidence is limited by small sample sizes, lack of comparators, and short follow-up durations. Currently, VNS devices are not FDA-approved for any of these indications and there is insufficient evidence to draw conclusions regarding the use of VNS for these conditions (Han, et al., 2025; Powers, et al., 2025; Dilixiati, et al., 2024; Courties, et al., 2021; Stegeman, et al., 2021; Errico, 2018; Reijmen, et al., 2018; Gold, et al., 2016; Zannad, et al., 2015).

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

According to a report by Nathan and Gutierrez (2018), the prevalence of epilepsy in nonwhite males is 1.3–2.2 times that of white males and in nonwhite females, it is 1.4–1.7 times that of white females. Between 1986 and 1990, the age adjusted prevalence rate of epilepsy for African Americans was 6.7 per 1,000 compared to 4.5 per 1,000 for whites. The prevalence rate for elderly Hispanic men was 15–18 per 1,000 compared to 12–16 per 1,000 for non-Hispanic men of a similar age group. African American and Hispanic individuals were less likely to receive surgical treatment, antiepileptic drugs (AEDs), and specialized care and more likely to receive care in an emergency room when compared to white individuals. The authors found that fear of treatment, access to care, communication barriers, education, trust between patient and physician, and social support are all contributing factors to these disparities.

In a post hoc analysis of the Human Epilepsy Project 2 (HEP2), Alcala-Zermeno et al. (2024) examined disparities in access to epilepsy surgery and neuromodulation therapies in the U.S. They report Vagus Nerve Stimulation (VNS) therapy was less utilized among Black or African American individuals compared to non-Hispanic Whites despite all participants being eligible for device implantation. Black/African American individuals had significantly lower odds of having a device compared to non-Black patients ($p=0.03$) while Hispanic/Latino participants had device usage rates similar to non-Hispanic/Latinos. Study limitations include small sample size limiting statistical comparisons across racial groups, recruitment from high-complexity sites which may underrepresented VNS patients typically treated in lower-complexity settings, and lack of data on whether patients were offered neuromodulation devices as part of their care. The study highlights racial disparities as a barrier to neuromodulation device use in treating drug-resistant epilepsy (DRE). Further research is needed to understand the root causes of these gaps.

In a 2025 policy statement from the American Heart Association (AHA) and American Stroke Association (ASA), Ifejika et al. highlight that while advances in stroke treatment have reduced mortality, they have led to an increase in survivors with functional impairments. The statement notes that individuals in rural areas face a higher risk of stroke, and post-stroke outcomes show higher rates of functional and cognitive impairments in underrepresented races or ethnicities (e.g., Black and Hispanic individuals). Additionally, lower socioeconomic status limits access to post-acute care and rehabilitation services. Although research on racial disparities in stroke rehabilitation is limited, existing studies show that non-Hispanic White patients are more likely to receive facility-based rehabilitation and have higher functional status scores at both admission and discharge compared to Black and Hispanic patients. Intensive inpatient rehabilitation (IRF) has been shown to improve functional outcomes compared with other settings. In a study of 1066 participants across 11 IRF facilities, Black and Hispanic patients had significantly lower Functional Independence Measure scores at 3 and 12 months compared to White patients. The authors emphasize the need for more studies to understand and address disparities in stroke rehabilitation and recovery.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	Vagus Nerve Stimulation (VNS) (160.18)	7/22/20
LCD	Local	No Local Coverage Determination found	NA

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

References

1. Aaronson ST, Sears P, Ruvuna F, Bunker M, Conway CR, Dougherty DD, et al. A 5-Year Observational Study of Patients With Treatment-Resistant Depression Treated With Vagus Nerve Stimulation or Treatment as Usual: Comparison of Response, Remission, and Suicidality. Am J Psychiatry. 2017 Jul 1;174(7):640-648.

2. Alcala-Zermeno JL, Fureman B, Grzeskowiak CL, Potnis O, Taveras M, Logan MW, Rybacki D, Friedman D, Lowenstein D, Kuzniecky R, French J; HEP2 investigators. Racial disparities in the utilization of invasive neuromodulation devices for the treatment of drug-resistant focal epilepsy. Epilepsia. 2024 May;65(5):e61-e66. doi: 10.1111/epi.17961. Epub 2024 Mar 20. PMID: 38506370.

3. American Psychological Association (APA). APA Clinical Practice Guideline for the treatment of depression across three age cohorts. Approved February 2019. Available at: https://www.apa.org/depression-guideline/guideline.pdf. Accessed on September 19, 2025.

4. Austelle CW, O'Leary GH, Thompson S, Gruber E, Kahn A, Manett AJ, Short B, Badran BW. A Comprehensive Review of Vagus Nerve Stimulation for Depression. Neuromodulation. 2022 Apr;25(3):309-315. doi: 10.1111/ner.13528. Epub 2021 Sep 6. PMID: 35396067; PMCID: PMC8898319.

5. Bottomley JM, LeReun C, Diamantopoulos A, Mitchell S, Gaynes BN. Vagus nerve stimulation (VNS) therapy in patients with treatment resistant depression: A systematic review and meta-analysis. Compr Psychiatry. 2019 Dec 12;98:152156.

6. Centers for Disease control and Prevention. (2020). Epilepsy. Accessed September 22, 2025. Available at URL address: https://www.cdc.gov/epilepsy/index.html

7. Centers for Medicare and Medicaid Services (CMS). Medicare Coverage Database. Accessed Sep 23, 2025. Available at URL address: https://www.cms.gov/medicare-coverage-database/search.aspx

8. Chan E, Mani AR. Assessing the therapeutic potential of vagus nerve stimulation in autoimmune diseases: A systematic review. Physiol Rep. 2025 Feb;13(3):e70230. doi: 10.14814/phy2.70230. PMID: 39903575; PMCID: PMC11793006.

9. Conway CR, Aaronson ST, Sackeim HA, George MS, Zajecka J, Bunker MT, Duffy W, Stedman M, Riva-Posse P, Allen RM, Quevedo J, Berger M, Alva G, Malik MA, Dunner DL, Cichowicz I, Banov M, Manu L, Nahas Z, Macaluso M, Mickey BJ, Sheline Y, Kriedt CL, Lee

YL, Gordon C, Shy O, Tran Q, Yates L, Rush AJ. Vagus nerve stimulation in treatment-resistant depression: A one-year, randomized, sham-controlled trial. Brain Stimul. 2025 May-Jun;18(3):676-689. doi: 10.1016/j.brs.2024.12.1191. Epub 2024 Dec 18. PMID: 39706521.

10. Conway CR, Kumar A, Xiong W, Bunker M, Aaronson ST, Rush AJ. Chronic Vagus Nerve Stimulation Significantly Improves Quality of Life in Treatment-Resistant Major Depression. J Clin Psychiatry. 2018 Aug 21;79(5).

11. Courties A, Berenbaum F, Sellam J. Vagus nerve stimulation in musculoskeletal diseases. Joint Bone Spine. 2021 May; 88(3):105149. Doi: 10.1016/j.jbspin.2021.105149. Epub 2021 Feb 3. PMID: 33548494.

12. Dawson J, Liu CY, Francisco GE, Cramer SC, Wolf SL, Dixit A, Alexander J, Ali R, Brown BL, Feng W, DeMark L, Hochberg LR, Kautz SA, Majid A, O'Dell MW, Pierce D, Prudente CN, Redgrave J, Turner DL, Engineer ND, Kimberley TJ. Vagus nerve stimulation paired with rehabilitation for upper limb motor function after ischaemic stroke (VNS-REHAB): a randomised, blinded, pivotal, device trial. Lancet. 2021 Apr 24;397(10284):1545-1553.

13. Department of Veterans Affairs/Department of Defense. Clinical Practice Guideline for the Management of Depressive Disorder. Version 4.0 – 2022. Accessed September 23, 2025. Available at URL address: https://www.healthquality.va.gov/guidelines/MH/mdd/VADODMDDCPGFinal508.pdf

14. Department of Veterans Affairs/Department of Defense. Clinical Practice Guideline for Management of Stroke Rehabilitation. Version 5.0 – 2024. Accessed September 25, 2025. Available at URL address: https://www.healthquality.va.gov/guidelines/Rehab/stroke/VADOD-2024-Stroke-Rehab-CPG-Full-CPG_final_508.pdf

15. Dibué M, Greco T, Spoor JKH, Tahir Z, Specchio N, Hänggi D, Steiger HJ, Kamp MA. Vagus nerve stimulation in patients with Lennox-Gastaut syndrome: A meta-analysis. Acta Neurol Scand. 2021 May;143(5):497-508.

16. Dibué-Adjei M, Brigo F, Yamamoto T, Vonck K, Trinka E. Vagus nerve stimulation in refractory and super-refractory status epilepticus - A systematic review. Brain Stimul. 2019 Sep-Oct;12(5):1101-1110.

17. Dilixiati S, Yan J, Qingzhuoga D, Song G, Tu L. Exploring Electrical Neuromodulation as an Alternative Therapeutic Approach in Inflammatory Bowel Diseases. Medicina (Kaunas). 2024 Apr 27;60(5):729. doi: 10.3390/medicina60050729. PMID: 38792911; PMCID: PMC11123282.

18. Errico JP. The Role of Vagus Nerve Stimulation in the Treatment of Central and Peripheral Pain Disorders and Related Comorbid Somatoform Conditions. In: Krames ES, Peckham PH, Rezai AR. Neuromodulation. 2nd ed. San Diego, CA: Academic Press; 2018. Ch 132. 1551-1564.

19. Feygina AA, Koshelyaevskaya YN, Dibué M, Voronkova KV, Klochkov MN, Koroleva NY, Ivanov SS, Bolshakova ES, Fatykhova EF. Efficacy and safety following two or more years of vagus nerve stimulation (VNS Therapy) in pediatric patients with drug-resistant

epilepsy enrolled in a Russian VNS Registry. Brain Behav. 2023 Jul;13(7):e3076. doi: 10.1002/brb3.3076. Epub 2023 May 30. PMID: 37254623; PMCID: PMC10338786.

20. Fraenkel L, Bathon JM, England BR, St. Clair EW, Arayssi T, Carandang K, Deane KD, Genovese M, Huston KK, Kerr G, Kremer J, Nakamura MC, Russell LA, Singh JA, Smith BJ, Sparks JA, Venkatachalam S, Weinblatt ME, Al-Gibbawi M, Baker JF, Barbour KE, Barton JL, Cappelli L, Chamseddine F, George M, Johnson SR, Kahale L, Karam BS, Khamis AM, Navarro-Millán I, Mirza R, Schwab P, Singh N, Turgunbaev M, Turner AS, Yaacoub S, Akl EA. 2021 American College of Rheumatology Guideline for the Treatment of Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2021 Jul;73(7):924-939. doi:10.1002/acr.24596. Accessed Dec 23, 2025. Available at URL address: https://rheumatology.org/clinical-practice-guidelines

21. Gelenberg AJ, Freeman MP, Markowitz JC, Rosenbaum JF, Thase ME, Trivedi MH, et al. American Psychiatric Association (APA). Practice guideline for the treatment of patients with major depressive disorder. 3rd Edition. Revise October 2010. Reaffirmed Oct 31, 2015. Accessed September 22, 2025. Available at URL address: https://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/mdd.pdf

22. Gold MR, Van Veldhuisen DJ, Hauptman PJ, Borggrefe M, Kubo SH, Lieberman RA, et al. Vagus Nerve Stimulation for the Treatment of Heart Failure: The INOVATE-HF Trial. J Am Coll Cardiol. 2016 Jul 12;68(2):149-58.

23. Goldstein LB. Ischemic Cerebrovascular Disease. In: Goldman L, Cooney KA. Goldman-Cecil Medicine. 27th ed. Philadelphia: Elsevier; 2024. 2464-2476.

24. Han HJ, Kim H, Kim DJ. Systematic review for VNS vs. pharmaceutical modulations for multifaceted neurological disorder management through cross-case, network meta-analysis. Brain Stimul. 2025 May-Jun;18(3):909-936. doi: 10.1016/j.brs.2025.04.007. Epub 2025 Apr 11. PMID: 40220956.

25. Ifejika NL, Awosika OO, Black T, Duncan PW, Harvey RL, Katz DI, Kimberley TJ, Lutz B, O'Neil F, Stein J, Yallapragada AV, Reeves MJ. Improving access to stroke rehabilitation and recovery: a policy statement from the American Heart Association/American Stroke Association. Stroke. 2025 Sep;56:e218–e233. doi: 10.1161.

26. Khan I, Shakir M, Vijayanarasimhan V, Lodhi BA, Parker JJ, Miller KJ, Khan M, Grewal SS, Ali R. Implantable Vagus Nerve Stimulator-Paired Neurorehabilitation for Upper Limb Function After Ischemic Stroke: Evidence From a Systematic Review and Meta-Analysis With Best Practice Recommendations. Neurosurgery. 2025 Jun 3. doi: 10.1227/neu.0000000000003545. Epub ahead of print. PMID: 40459273.

27. Kilgard MP, Rennaker RL, Alexander J, Dawson J. Vagus nerve stimulation paired with tactile training improved sensory function in a chronic stroke patient. NeuroRehabilitation. 2018;42(2):159-165

28. Kimberley TJ, Cramer SC, Wolf SL, Liu C, Gochyyev P, Dawson J; VNS-REHAB Trial Group. Long-Term Outcomes of Vagus Nerve Stimulation Paired With Upper Extremity Rehabilitation After Stroke. Stroke. 2025 Aug;56(8):2255-2265. doi: 10.1161/STROKEAHA.124.050479. Epub 2025 May 7. PMID: 40329913.

29. Kumar A, Bunker MT, Aaronson ST, Conway CR, Rothschild AJ, Mordenti G, Rush AJ. Durability of symptomatic responses obtained with adjunctive vagus nerve stimulation in treatment-resistant depression. Neuropsychiatr Dis Treat. 2019 Feb 13;15:457-468. doi: 10.2147/NDT.S196665. PMID: 30858703; PMCID: PMC6387594.

30. Lichtenstein GR, Loftus EV, Afzali A, Long MD, Barnes EL, Isaacs KL, Ha CY. ACG Clinical Guideline: Management of Crohn's Disease in Adults. Am J Gastroenterol. 2025;120(6):1225-1264. doi:10.14309/ajg.0000000000003465. Accessed Dec 23, 2025. Available at URL address: https://journals.lww.com/ajg/Pages/ACG-Clinical-Guidelines.aspx

31. Liu J, Zheng K, Dong L, Lin J, Zhang C, Xie Y, Wang Y. Clinical applications and mechanisms of vagus nerve stimulation in the treatment of immune diseases: a review. Int J Surg. 2025 Dec 1;111(12):9496-9506. doi: 10.1097/JS9.0000000000003160. Epub 2025 Aug 8. PMID: 40788025; PMCID: PMC12695341

32. Lombo, L.E., Tejada-Perdomo, J.H., Ramos-Castaneda, J.A. and Garcia, R.G. (2025), Vagus Nerve Stimulation in Autoimmune Conditions: A Systematic Review. ACR Open Rheumatology, 7: e70137. https://doi.org/10.1002/acr2.70137

33. Mandalaneni K, Rayi A. Vagus Nerve Stimulator. [Updated 2023 Aug 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK562175/

34. McAllister-Williams RH, Sousa S, Kumar A, Greco T, Bunker MT, Aaronson ST, Conway CR, Rush AJ. The effects of vagus nerve stimulation on the course and outcomes of patients with bipolar disorder in a treatment-resistant depressive episode: a 5-year prospective registry. Int J Bipolar Disord. 2020 May 2;8(1):13. doi: 10.1186/s40345-020-0178-4. PMID: 32358769; PMCID: PMC7195501.

35. McIntyre RS, Alsuwaidan M, Baune BT, Berk M, Demyttenaere K, Goldberg JF, Gorwood P, Ho R, Kasper S, Kennedy SH, Ly-Uson J, Mansur RB, McAllister-Williams RH, Murrough JW, Nemeroff CB, Nierenberg AA, Rosenblat JD, Sanacora G, Schatzberg AF, Shelton R, Stahl SM, Trivedi MH, Vieta E, Vinberg M, Williams N, Young AH, Maj M. Treatment-resistant depression: definition, prevalence, detection, management, and investigational interventions. World Psychiatry. 2023 Oct;22(3):394-412. doi: 10.1002/wps.21120. PMID: 37713549; PMCID: PMC10503923.

36. Morris GL 3rd, Gloss D, Buchhalter J, Mack KJ, Nickels K, Harden C. Evidence-based guideline update: Vagus nerve stimulation for the treatment of epilepsy: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2013 Aug 28. Reaffirmed July 19, 2025. Accessed Sep 23, 2025. Available at URL address: https://www.aan.com/Guidelines/Home/GuidelineDetail/618

37. Muniyandi M, Chelvanayagam K, Salam SA, Vadamalai S, Rajsekar K, Ramachandran R. Significant reduction of seizure frequency in patients with drug-resistant epilepsy by vagus nerve stimulation: Systematic review and meta-analysis. Epilepsy Res. 2025 Feb;210:107510. doi: 10.1016/j.eplepsyres.2025.107510. Epub 2025 Jan 9. Erratum in: Epilepsy Res. 2025 Mar;211:107519. doi: 10.1016/j.eplepsyres.2025.107519. PMID: 39809131.

38. Nathan CL, Gutierrez C. FACETS of health disparities in epilepsy surgery and gaps that need to be addressed. Neurol Clin Pract. 2018 Aug;8(4):340-345.

39. Panebianco MD, Rigby A, Weston J, Marson AG. Vagus nerve stimulation for focal seizures. Cochrane Database of Systematic Reviews 2015, Issue 4. Art. No.: CD002896. Last updated July 14, 2022.

40. Powers MB, Hays SA, Rosenfield D, Porter AL, Gallaway H, Chauvette G, Smits JAJ, Warren AM, Douglas M, Naftalis R, Wigginton JG, Foreman M, Kilgard MP, Rennaker RL. Vagus nerve stimulation therapy for treatment-resistant PTSD. Brain Stimul. 2025 May-Jun;18(3):665-675. doi: 10.1016/j.brs.2025.03.007. Epub 2025 Mar 15. PMID: 40097094.

41. Reijmen E, Vannucci L, De Couck M, De Grève J, Gidron Y. Therapeutic potential of the vagus nerve in cancer. Immunol Lett. 2018 Oct;202:38-43.

42. Robbins MS, Starling AJ, Pringsheim TM, Becker WJ, Schwedt TJ. Treatment of Cluster Headache: The American Headache Society Evidence-Based Guidelines. Headache. 2016 Jul;56(7):1093-106.

43. Rubin DT, Ananthakrishnan AN, Siegel CA, Barnes EL, Long MD. ACG Clinical Guideline Update: Ulcerative Colitis in Adults. Am J Gastroenterol. 2025;120(6):1187-1224. doi:10.14309/ajg.0000000000003463. Accessed Dec 23, 2025. Available at URL address: https://journals.lww.com/ajg/Pages/ACG-Clinical-Guidelines.aspx

44. Rush AJ, Conway CR, Aaronson ST, George MS, Riva-Posse P, Dunner DL, Zajecka J, Bunker MT, Quevedo J, Allen RM, Alva G, Luing H, Nahas Z, Manu L, Bennett JI, Mickey BJ, Becker J, Sheline Y, Cusin C, Murrough JW, Reeves K, Rosenquist PB, Lee YL, Majewski S, Way J, Olin B, Sackeim HA. Effects of vagus nerve stimulation on daily function and quality of life in markedly treatment-resistant major depression: Findings from a one-year, randomized, sham-controlled trial. Brain Stimul. 2025 May-Jun;18(3):690-700. doi: 10.1016/j.brs.2024.12.1187. Epub 2024 Dec 18. PMID: 39701918.

45. Ryvlin P, Gilliam FG, Nguyen DK, Colicchio G, Iudice A, Tinuper P, et al. The long-term effect of vagus nerve stimulation on quality of life in patients with pharmacoresistant focal epilepsy: the PuLsE (Open Prospective Randomized Long-term Effectiveness) trial. Epilepsia. 2014 Jun;55(6):893-900.

46. SetPoint Medical. SetPoint Medical Announces CMS Transitional Pass-Through Payment Approval for the SetPoint System, the Breakthrough Neuroimmune Modulation Platform. Valencia (CA): SetPoint Medical; Nov 24, 2025. Accessed Dec 22, 2025. Available at URL address: https://setpointmedical.com/setpoint-medical-announces-cms-transitional-pass-through-payment-approval-for-the-setpoint-system-the-breakthrough-neuroimmune-modulation-platform/

47. Smith JH. Acute treatment of migraine in adults. Literature review current through: Oct 2019a. Last updated August 1, 2018. In: UpToDate, Swanson JW (Ed), UpToDate, Waltham, MA.

48. Smith JH. Preventive treatment of migraine in adults. Literature review current through: Oct 2019b. Last updated August 28, 2018. In: UpToDate, Swanson JW (Ed), UpToDate, Waltham, MA.

49. Stegeman I, Velde HM, Robe PAJT, Stokroos RJ, Smit AL. Tinnitus treatment by vagus nerve stimulation: A systematic review. PLoS One. 2021 Mar 11; 16(3):e0247221. Doi: 10.1371/journal.pone.0247221. PMID: 33705401; PMCID: PMC7951891.

50. Suller Marti A, Verner R, Keezer M, Andrade A, Veilleux M, Myers K, Giannicola G, Nichol K, G Burneo J; CORE-VNS Registry Group. Reduction of generalized tonic-clonic seizures following vagus nerve stimulation therapy: CORE-VNS Study 24-month follow-up. Epilepsia. 2025 Jul;66(7):2307-2314. doi: 10.1111/epi.18371. Epub 2025 Apr 1. PMID: 40167365; PMCID: PMC12291022.

51. Tesser JRP, Crowley AR, Box EJ, June JP, Wickersham PB, Valenzuela GJ, Gaylis NB, Lam GKW, Pacheco LA, Ridley DJ, Pinto-Patarroyo GP, Novack SN, Churchill MA, Kohler M, Lee EC, Pando JA, Parris GR, Peterson JR, Shah T, Singhal AK, Vuong V, Levine YA, Evangelista ML, Derosier AA, Curtis JR, Richardson RM, Chernoff D. Vagus nerve–mediated neuroimmune modulation for rheumatoid arthritis: a pivotal randomized controlled trial. Nature Medicine. 2025;31(?):1-??. doi:10.1038/s41591-025-04114-7.

52. U.S. Food Drug Administration (FDA). Premarket approval (PMA) database. Product code(s): LYJ, MUZ, QPY, SFJ. Page Last Updated: Dec 22, 2025. Accessed Dec 22, 2025. Available at URL address: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm

53. Wang L, Xu Q, Luo M, Xing X, Wang J, Liang Y, Zhang J, Sheng R, Niu S, Wang Y. Vagus nerve stimulation in various stages of stroke and associated functional impairments: A review. Neuroscience. 2025 Jun 21;577:80-113. doi: 10.1016/j.neuroscience.2025.04.037. Epub 2025 May 2. PMID: 40320233.

54. Winstein CJ, Stein J, Arena R, Bates B, Cherney LR, Cramer SC, Deruyter F, Eng JJ, Fisher B, Harvey RL, Lang CE, MacKay-Lyons M, Ottenbacher KJ, Pugh S, Reeves MJ, Richards LG, Stiers W, Zorowitz RD. Guidelines for adult stroke rehabilitation and recovery: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2016 Jun;47(6):e98–e169. Accessed Oct 2, 2025. Available at URL address: https://www.ahajournals.org/doi/pdf/10.1161/STR.0000000000000098

55. Zannad F, De Ferrari GM, Tuinenburg AE, Wright D, Brugada J, Butter C, et al. Chronic vagal stimulation for the treatment of low ejection fraction heart failure: results of the Neural Cardiac Therapy for Heart Failure (NECTAR-HF) randomized controlled trial. Eur Heart J. 2015 Feb 14;36(7):425-33.

Revision Details

Type of Revision	Summary of Changes	Date
Focused Review	• Revised policy statement for not medically necessary indications	2/15/2026
Annual Review	• Revised policy statement for implantable VNS for "other" indications. • Removed policy statement for transcutaneous stimulation (tVNS). • Updated to new formatting standards.	12/15/2025
Focused Review	• Addition of new code 0908T. • No clinical policy statement changes.	2/15/2025

Revision	• No clinical policy statement changes.	12/15/2024
Revision	• Removed policy statement for replacement/revision of an implantable vagus nerve stimulator and/or leads	12/15/2023