Clinical Policy: Vagus Nerve Stimulation

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Effective Date: 01/18
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Coding Implications
Revision Log

Description

Vagus nerve stimulation (VNS) has been used in the treatment of epilepsy and has been studied for the treatment of refractory depression and other indications. Electrical pulses are delivered to the cervical portion of the vagus nerve by an implantable device called a neurocybernetic prosthesis. Chronic intermittent electrical stimulation of the left vagus nerve is designed to treat medically refractory epilepsy.[1] VNS has recently been introduced and approved by the Food and Drug Administration (FDA) as an adjunctive therapy for treatment-resistant major depression.[2]

Policy/Criteria

I. It is the policy of PHW that vagus nerve stimulation (VNS) is **medically necessary** in members/enrollees with medically refractory seizures who meet all of the following:
- **A.** Diagnosis of focal onset (formerly partial onset) seizures or generalized onset seizures;
- **B.** Intractable epilepsy (both):
  1. Failure of at least one year of adherent therapy of at least two anti-seizure drugs;
  2. Continued seizures which have a major impact on activities of daily living;
- **C.** Not a suitable candidate for, is opposed to, or has failed epilepsy surgery;
- **D.** Request is for an FDA approved device.

II. It is the policy of PHW that the safety and efficacy of VNS therapy has not been proven for any other conditions, including but not limited to the following:
- **A.** Refractory (treatment resistant) major depression or bipolar disorder;
- **B.** Headaches;
- **C.** Cognitive impairment associated with Alzheimer's disease;
- **D.** Addiction;
- **E.** Anxiety Disorders;
- **F.** Autism;
- **G.** Eating Disorders;
- **H.** Cancer;
- **I.** Crohn's Disease;
- **J.** Essential trauma;
- **K.** Fibromyalgia;
- **L.** Heart failure;
- **M.** Impaired glucose tolerance/pre-diabetes;
- **N.** Inflammation;
- **O.** Overweight and obesity;
- **P.** Obsessive-compulsive disorder;
- **Q.** Panic disorder;
- **R.** Post-traumatic stress disorder;
- **S.** Prader-Willi Syndrome;
- **T.** Sjogren's Syndrome;
- **U.** Rheumatoid arthritis;
- **V.** Schizophrenia;

W. Sleep disorders;
X. Stroke;
Y. Tinnitus;
Z. Tourette's syndrome;
AA. Traumatic brain injury.

III. It is the policy of PHW that the current research does not support the use of the following types of VNS therapy over other currently available alternatives, due to the lack of large, high-quality studies supporting their use:
A. Aspire SR Model 106 (Cyberonics) for VNS;
B. Transcutaneous VNS or active auricular transcutaneous electrical nerve stimulation.

Background

The vagus nerve stimulator is a pacemaker-like device implanted under the skin in the left side of the chest through a small incision, with a second small incision made at the base of the neck.[3] The surgery is performed primarily by a neurosurgeon over approximately 45 to 90 minutes under general anesthesia as an outpatient surgery. There is a small risk of infection, along with additional surgical risks that include inflammation or pain at the incision site, damage to nearby nerves and nerve constriction.[37]

Focal (Partial) Seizures

Several studies have been done evaluating the safety and efficacy of vagus nerve stimulation (VNS) for treatment of epilepsy. A randomized active-control trial known as the E05 study found that 94 patients (of the total 254 patients in the study) receiving high stimulation showed an average reduction in seizure frequency, compared to baseline, of 28% versus 15% reduction in the 102 patients receiving low stimulation. A total of 310 patients completed the E03 and E05 double-blinded trials. Mean decline of seizure frequency overall was about 25 to 30% compared to baseline. Clinical experience has shown that improvement in seizures is maintained, or may even increase over time, but these data are based on uncontrolled observations. Side effects in both studies were similar and included hoarseness and occasional shortness of breath.[1]

Although questions regarding patient selection criteria, optimal stimulation parameters, and cost-effectiveness in the United States remain under investigation, there is sufficient evidence regarding the benefit and safety of VNS to conclude that VNS may improve health outcomes in patients with medically refractory focal-onset seizures who are not suitable candidates for surgery or in whom surgical treatment has failed.[4]

Generalized seizures

Study results suggest VNS may be effective for generalized epilepsy. However, case series and observational studies constitute the majority of available evidence. Although VNS is not currently approved by the Food and Drug Administration (FDA) for the treatment of generalized seizures, it is often used in children and other patients and in Europe is approved as adjunct therapy for epileptic disorders predominantly characterized by generalized or focal seizures that are refractory to antiseizure medications.[1] The National Institute for Health and Care Excellence (NICE) recommends VNS for focal and generalized seizures as an adjunctive therapy in patients who are refractory to antiseizure medications and who are not suitable for resective surgery.[5,6]

Additionally, the Scottish Intercollegiate Guidelines Network (SIGN) guidelines recommend VNS for epilepsy in patients unsuitable for resective surgery without stipulating seizure type.[7]

Depression
VNS was FDA-approved for treatment of resistant depression in 2005. However, VNS has no rigorous research data proving it is efficacious for treatment-resistant, unipolar major depression. Open-label studies suggest VNS may be effective; however, these are at risk for bias due to placebo effects. Two randomized controlled trials (RCTs) of VNS for depression found no benefit, and one of these RCTSs had outcomes comparable for active and sham treatment (response rates of 15 versus 10 percent). In addition, there is a lack of thorough safety data for the use of VNS in depression.[2]

Other Investigational Indications
Ongoing research efforts continue to investigate the role of VNS for the treatment of a variety of indications, including but not limited to cognitive deficits in Alzheimer's disease, resistant obesity, and headaches. Data supporting the long-term safety and efficacy from large clinical trials of VNS for the treatment of these indications, however, continue to be lacking.[14,15,38,39]

AspireSR Model 106 (Cyberonics) for Vagus Nerve Stimulation
The AspireSR Model 106 (Cyberonics Inc.) received FDA Premarket Approval (PMA) in February 2014. The newest modification to the implantable VNS device detects tachycardia heart rates, which may be associated with an impending seizure, and automatically delivers stimulation to the vagus nerve. Like its predecessors, the AspireSR can also deliver stimulation in the normal and magnet modes. However, when programmed for AutoStim mode, the AspireSR requires no patient interaction to trigger the delivery of electrical stimulation. The AutoStim mode should not be used in patients with significant arrhythmias being treated with pacemakers and/or an implantable defibrillator, beta-blockers, or any other treatment that may impact the intrinsic heart rate.[8,9]

A few small, preliminary studies and case reports have evaluated the AspireSR Model 106, and have shown positive results.[8,9,10] However, there is insufficient evidence to establish the safety and efficacy of the AspireSR Model 106 in reducing seizures until further, high quality trials establish its clinical value.

Transcutaneous (non-implantable) Vagus Nerve Stimulation
Transcutaneous vagus nerve stimulation (tVNS) has been proposed as a noninvasive alternative to implantable VNS for a variety of indications, including, but not limited to epilepsy, major depression, post-traumatic stress syndrome (PTSD), chronic tinnitus, and headaches. Currently, there are two main ways to apply tVNS. One is to apply stimulation on the ear and the other is cervical noninvasive VNS, superficially applying stimulation in the vicinity of the vagus nerve using a specially designed device, (e.g., gammaCore, Phoenix). Noninvasive auricular tVNS stimulates the afferent auricular branch of the vagus nerve located medial of the tragus at the entry of the acoustic meatus. Given that the right vagal nerve has efferent fibers to the heart, tVNS is safe to be performed only in the left ear. tVNS has been proposed to study cognitive functioning in patients with epilepsy and major depression. The rationale is that direct stimulation of the afferent nerve fibers on the ear area with afferent vagus nerve distribution

should produce a similar effect as classic VNS in reducing depressive symptoms without the burden of surgical intervention. A noninvasive, transcutaneous vagal nerve stimulator has been in use in Europe. Although no randomized studies have been done in patients with epilepsy, it appears promising in one pilot study.[11] Small studies have shown positive results with tVNS for the treatment of depression.[12,13] Additional, larger, peer-reviewed studies, with longer follow-up are necessary to determine the long-term safety and efficacy of transcutaneous VNS for depression.

gammaCore Sapphire™ (ElectroCore, LLC) is a hand-held prescription device that is placed externally on the side of the neck in the vicinity of the vagus nerve to deliver a low voltage electric signal to the nerve's afferent fibers.[14] gammaCore has received FDA approval for the treatment of both episodic cluster and migraine headaches and more recently for the prevention of cluster headaches (CH). gammaCore is under investigation for the treatment of post-traumatic stress syndrome (PTSD).[40] gammaCore delivers up to 30 stimulations in a 24-hour period, each lasting two minutes. The patient controls the intensity level. Once the maximum daily number of treatments has been reached, the device will not deliver any more treatments until the following 24-hour period. A gammaCore refill card is used to load the device with days of therapy based on a healthcare provider's prescription.[14]

In the randomized PRESTO study, noninvasive vagus nerve stimulation (nVNS.) was superior to sham in the treatment of episodic migraine for pain freedom at 30 minutes and 60 minutes after the first treated attack.[15] In both the ACT1 and ACT2 trials, nVNS was superior to sham therapy in episodic CH but not in chronic CH.[2,15] Another 2020 randomized, double-blind, sham-controlled clinical trial showed when comparing nVNS with sham, no statistically significant differences were found with regards to the primary endpoint of pain freedom at 120 minutes, although differences were found with various secondary endpoints and post hoc analysis.[16]

Preliminary clinical trials of nVNS in various primary headache disorders are encouraging, but, for future studies, it is important to conduct large, properly blinded and controlled trials by independent researchers.[14] Additionally, most studies nVNS devices enrolled participants who did not respond sufficiently to oral drug treatment; thus, the role of neurostimulation in an average population of migraine patients remains unknown.[17]

The Phoenix is a transcutaneous auricular vagus nerve stimulation (tVNS) system in development for the treatment of post-traumatic stress disorder symptoms by delivering electrical stimulation to the pinna of the ear using a proprietary soft silicone conductive earbud connected to a programmable handheld control device. The control software uses an adaptive response algorithm and has multiple treatment modes to allow adjustment of stimulation parameters to customize treatment for individual members. There are no published studies reporting on the use of the Phoenix transcutaneous auricular vagus nerve stimulation (tVNS) system for treatment of PTSD. Published evidence is limited to a preliminary feasibility trial that validated the increase in parasympathetic nerve activity with tVNS during a tilt test and a startle response test. Results from larger published randomized trials that compare the Phoenix tVNS system to usual care in patients with PTSD are required to demonstrate safety and effectiveness for the treatment of PTSD.[40]

The American Headache Society position statement on integrating new migraine treatments into clinical practice note that empirically validated behavioral treatments with Grade A evidence for the prevention of migraine, including cognitive behavioral therapy, biofeedback, and relaxation therapies, should be considered in the management of migraine. These modalities may also be used alone or in addition to pharmacologic treatment. They note further that several noninvasive devices have been developed and approved by the FDA for the treatment of patients with migraines (i.e., single-pulse transcranial magnetic stimulation, electrical trigeminal nerve stimulation and nVNS).[18] Patients who prefer nondrug therapies, and those who have failed to respond to, have contraindications to, or poor tolerability with pharmacotherapy may be candidates for neuromodulation.[19]

Per UpToDate, "There are several promising but unproven methods using neurostimulation to treat medically refractory cluster headache, including sphenopalatine ganglion stimulation, occipital nerve stimulation, noninvasive VNS, and deep brain stimulation. All are investigational and require further study to confirm long-term benefit and safety."[15]

Removal of Implant
Removal of a vagus nerve stimulator may become necessary due to device malfunction, unbearable side effects, signs of infections, or a lack of efficacy. The device can be turned off in the physician's office if the patient feels it is not helping or if the patient cannot tolerate the stimulation. If the device needs to be removed, only the pulse generator is removed, as attempting to remove the electrodes from around the nerve can cause damage and is not recommended.[36]

Coding Implications
This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2022, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

CPT®* Codes	Description
61885	Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array
61886	Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to two or more electrode arrays
61888	Revision or removal of cranial neurostimulator pulse generator or receiver
64553	Percutaneous implantation of neurostimulator electrodes; cranial nerve
64568	Incision for implantation of cranial nerve (eg, vagus nerve) neurostimluator electrode array and pulse generator
64569	Revision or replacement of cranial nerve (eg, vagus nerve) neurostimulator electrode array, including connection to existing pulse generator

CPT®* Codes	Description
64570	Removal of cranial nerve (eg, vagus nerve) neurostimulator electrode array and pulse generator

HCPCS Codes that Support Coverage Criteria

HCPCS Codes	Description
C1767	Generator, neurostimulator (implantable), nonrechargeable
C1778	Lead, neurostimulator (implantable)
C1816	Receiver and/or transmitter, neurostimulator (implantable)
C1883	Adaptor/extension, pacing lead or neurostimulator lead (implantable)
L8680	Implantable neurostimulator electrode, each
L8681	Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
L8682	Implantable neurostimulator radiofrequency receiver
L8683	Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver
L8685	Implantable neurostimulator pulse generator, single array , rechargeable, includes extension
L8686	Implantable neurostimulator pulse generator, single array, nonrechargeable, includes extension
L8687	Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
L8688	Implantable neurostimulator pulse generator, dual array, nonrechargeable, includes extension
L8689	External recharging system for battery (internal) for use with implanted neurostimulator, replacement only

HCPCS Codes that Do Not Support Coverage Criteria

HCPCS Codes	Description
K1020	Noninvasive vagus nerve stimulator

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Developed PA Policy	11/17	1/18
Changed "partial onset" to "focal onset" throughout to reflect seizure classification changes made by the International League Against Epilepsy in 2017. References reviewed and updated.	08/18	
Updated background with additional information on non-implantable VNS. References reviewed and updated.	03/19	
References reviewed and updated. Added CPT code-61888. Added ICD-10 code, G40.311 Specialist review.	05/2020	

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Added additional investigational indications for VNS to section II. References reviewed and updated. Removed ICD-10 Codes: G40.001, G40.009, G40.201, G40.209, G40.309, G40.A09, G40.409, G40.509, G40.802, G40.909, G40.911 and G40.919. Added ICD-10: G40.813, G40.814. Added new HCPCs code K1020 to a new table of HCPCS codes that do not support coverage criteria. "Experimental/investigational" verbiage replaced with descriptive language in policy statement II and III. Replaced "member" with "member/enrollee."	06/2021	
Annual review. Changed "review date" in the header to "date of last revision" and "date" in the revision log header to "revision date." Background updated with additional study on nVNS for migraine headaches. References reviewed and updated. Reviewed by specialist.	07/18/2022	
Annual review. Added opposition to surgery as a possibility and removed "resective" in I.C. Additional minor rewording with no clinical significance made in Criteria section. Background updated with no impact on criteria. References reviewed and updated.	12/8/2022	
Annual review completed. Removed II.B. "Obesity". Additional minor rewording with no clinical significance. Background updated; moved "Removal of implant" section to background. ICD-10 Diagnosis code table removed. References reviewed and updated. External specialist reviewed.	08/23	

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