Clinical Policy: Vagus Nerve Stimulation

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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. It has recently been introduced and approved by the FDA as an adjunctive therapy for treatment-resistant major depression.

Policy/Criteria

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

II. It is the policy of PHW that VNS therapy is considered **investigational** for any other conditions, including but not limited to the following, because the evidence is limited supporting its safety and efficacy:
- **A.** Refractory (treatment resistant) major depression or bipolar disorder;
- **B.** Obesity;
- **C.** Headaches;
- **D.** Cognitive impairment associated with Alzheimer's disease.

III. It is the policy of PHW that the following types of VNS therapy are considered **investigational** due to the lack of large, high-quality studies supporting their use:
- **A.** Aspire SR Model 106 (Cyberonics) for vagus nerve stimulation;
- **B.** Transcutaneous VNS or active auricular transcutaneous electrical nerve stimulation.

Removal of Implant
Less than 0.5 percent of all patients have had the device removed. It 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.

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. The surgery is performed under local, regional, or general anesthesia and lasts 45 minutes to two

hours. Most often it is performed as an outpatient surgery but some patients need to stay in the hospital overnight following surgery.

Partial (focal) seizures
Several studies have been done evaluating the safety and effectiveness of vagus nerve stimulation 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 25-30% 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.

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 partial-onset seizures who are not suitable candidates for surgery or in whom surgical treatment has failed.

Generalized seizures
Study results suggest VNS may be effective for generalized epilepsy (Karceski & Schachter, 2015). However, case series and observational studies constitute the majority of available evidence. Although VNS is not currently FDA approved 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. In addition, the National Institute for Health and Care Excellence (NICE) recommends VNS for focal and generalized seizures, and the Scottish Intercollegiate Guidelines Network (SIGN) guidelines recommend VNS for epilepsy in patients unsuitable for respective surgery without stipulating seizure type.

Depression
VNS was FDA-approved for treatment 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. The one randomized trial of VNS for depression found no benefit, with outcomes comparable for active and sham treatment (response rates of 15 vs. 10 percent). In addition, there is a lack of thorough safety data for the use of VNS in depression.

Other Investigational Indications
Ongoing research efforts continue to investigate the role of vagus nerve stimulation (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.

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 vagus nerve stimulation (VNS) implant 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.

A few small, preliminary studies and case reports have evaluated the AspireSR Model 106, and have shown positive results (Boon et al., 2015; Fisher et al., 2015; Schneider et al., 2015; Hampel et al, 2015). 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 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, 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). 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.[18] Small studies have shown positive results with tVNS for the treatment of depression (Hein et al, 2013; Fang et al, 2016). 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. 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 delivers up to 30 stimulations in a 24-hour period, each lasting 2 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. gammaCore is rechargeable and includes a charging case to charge the device. A gammaCore refill card is used to load the device with days of therapy based on a healthcare provider's prescription.

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. [29] In both the ACT1 and ACT2 trials, nVNS was superior to sham therapy in episodic CH but not in chronic CH. [31,32] Preliminary clinical trials of nVNS in various primary headache disorders are encouraging, however, well-designed randomized controlled trials with larger sample size and long-term follow-up regarding safety and benefit is warranted. In addition, patient selection criteria needs to be defined.

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 migraine.(i.e., single-pulse transcranial magnetic stimulation, electrical trigeminal nerve stimulation and nVNS.) 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.[33]

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."

Coding Implications

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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
64553	Percutaneous implantation of neurostimulator electrodes; cranial nerve
64568	Incision for implantation of cranial nerve (eg, vagus nerve) neurostimluator electrode array and pulse generator

CPT®* Codes	Description
64569	Revision or replacement of cranial nerve (eg, vagus nerve) neurostimulator electrode array, including connection to existing pulse generator
64570	Removal of cranial nerve (eg, vagus nerve) neurostimulator electrode array and pulse generator

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

ICD-10-CM Diagnosis Codes that Support Coverage Criteria

ICD-10-CM Code	Description
G40.001	Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, not intractable, with status epilepticus
G40.009	Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, not intractable, without status epilepticus
G40.011	Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, with status epilepticus
G40.019	Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, intractable, without status epilepticus

ICD-10-CM Code	Description
G40.111	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, intractable, with status epilepticus
G40.119	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, intractable, without status epilepticus
G40.201	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, not intractable, with status epilepticus
G40.209	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, not intractable, without status epilepticus
G40.211	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable, with status epilepticus
G40.219	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with complex partial seizures, intractable, without status epilepticus
G40.309	Generalized idiopathic epilepsy and epileptic syndromes, not intractable, without status epilepticus
G40.319	Generalized idiopathic epilepsy and epileptic syndromes, intractable, without status epilepticus
G40.A09	Absence epileptic syndrome, not intractable, without status epilepticus
G40.A11	Absence epileptic syndrome, intractable, with status epilepticus
G40.A19	Absence epileptic syndrome, intractable, without status epilepticus
G40.409	Other generalized epilepsy and epileptic syndromes, not intractable, without status epilepticus
G40.411	Other generalized epilepsy and epileptic syndromes, intractable, with status epilepticus
G40.419	Other generalized epilepsy and epileptic syndromes, intractable, without status epilepticus
G40.509	Epileptic seizures related to external causes, not intractable, without status epilepticus
G40.802	Other epilepsy, not intractable, without status epilepticus
G40.803	Other epilepsy, intractable, with status epilepticus
G40.804	Other epilepsy, intractable, without status epilepticus
G40.909	Epilepsy, unspecified, not intractable, without status epilepticus
G40.911	Epilepsy, unspecified, intractable, with status epilepticus
G40.919	Epilepsy, unspecified, intractable, without status epilepticus

Reviews, Revisions, and Approvals	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	

Reviews, Revisions, and Approvals	Date	Approval Date
Updated background with additional information on non-implantable VNS. References reviewed and updated.	03/19	

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