

# Clinical Policy: Vagus Nerve Stimulation

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## 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 partial-onset seizures or generalized 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

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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 (Karciski & 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 a 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.

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#### *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*

Active auricular transcutaneous electrical nerve stimulation is also referred to as transcutaneous vagus nerve stimulation (tVNS). Noninvasive, 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. The device stimulates the auricular branch of the vagus nerve. It does this via a small earphone-like stimulator. Although no randomized studies have been done in patients with epilepsy, it appears promising in one pilot study (Bauer et al, 2016). 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.

#### **Coding Implications**

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<b>CPT®*</b> <b>Codes</b>	<b>Description</b>
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) neurostimulator electrode array and pulse generator
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

<b>HCPCS</b> <b>Codes</b>	<b>Description</b>
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**

<b>ICD-10- CM Code</b>	<b>Description</b>
G40.001	Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, not intractable, with status epilepticus

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ICD-10-CM Code	Description
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
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

ICD-10-CM Code	Description
G40.919	Epilepsy, unspecified, intractable, without status epilepticus

Reviews, Revisions, and Approvals	Date	Approval Date

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