

Protocol

Vagus Nerve Stimulation

(70120)

Medical Benefit		Effective Date: 01/01/15	Next Review Date: 11/19
Preauthorization	No	Review Dates: 01/07, 05/08, 11/08, 03/09, 01/10, 01/11, 01/12, 01/13, 01/14, 11/14, 11/15, 11/16, 11/17, 11/18	

Preauthorization is not required.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

Populations	Interventions	Comparators	Outcomes
Individuals: • With seizures refractory to medical treatment	Interventions of interest are: • Vagus nerve stimulation	Comparators of interest are: • Standard of care: antiepileptic drugs or resective surgery	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes
Individuals: • With treatment-resistant depression	Interventions of interest are: • Vagus nerve stimulation	Comparators of interest are: • Standard of care : antidepressant drugs	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes
Individuals: • With chronic heart failure • With upper-limb impairment due to stroke	Interventions of interest are: • Vagus nerve stimulation	Comparators of interest are: • Standard of care: medication management and physical rehabilitation	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes
Individuals: • With other neurologic conditions (e.g., essential tremor, headache, fibromyalgia, tinnitus or autism)	Interventions of interest are: • Vagus nerve stimulation	Comparators of interest are: • Standard of care: medication and behavioral therapy	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes
Individuals: • With episodic cluster headache	Interventions of interest are: • Transcutaneous vagus nerve stimulation	Comparators of interest are: • Standard of care: medication	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes
Individuals: • With other neurologic, psychiatric, or metabolic disorders	Interventions of interest are: • Transcutaneous vagus nerve stimulation	Comparators of interest are: • Standard of care: medication and behavioral therapy	Relevant outcomes include: • Symptoms • Change in disease status • Functional outcomes

DESCRIPTION

Stimulation of the vagus nerve can be performed using a pulsed electrical stimulator implanted within the carotid artery sheath. This technique has been proposed as a treatment for refractory seizures, depression, and

other disorders. There are also devices available that are implanted at different areas of the vagus nerve. This protocol also addresses devices that stimulate the vagus nerve transcutaneously.

SUMMARY OF EVIDENCE

VAGUS NERVE STIMULATION

For individuals who have seizures refractory to medical treatment who receive vagus nerve stimulation (VNS), the evidence includes randomized controlled trials (RCTs) and multiple observational studies. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCTs have reported significant reductions in seizure frequency for patients with partial-onset seizures. The uncontrolled studies have consistently reported large reductions in a broader range of seizure types in both adults and children. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals who have treatment-resistant depression who receive VNS, the evidence includes an RCT, non-randomized comparative studies, and case series. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCT only reported short-term results and found no significant improvement in the primary outcome. Other available studies are limited by small sample sizes, potential selection bias, and lack of a control group in the case series. The evidence is insufficient to determine the effects of the technology on health outcomes.

OTHER CONDITIONS

For individuals who have chronic heart failure who receive VNS, the evidence includes RCTs and case series. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCTs evaluating chronic heart failure did not show significant improvements in the primary outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have upper-limb impairment due to stroke who receive VNS, the evidence includes a single pilot study. Relevant outcomes are symptoms, change in disease status, and functional outcomes. This pilot study has provided preliminary support for improvement in functional outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have other neurologic conditions (e.g., essential tremor, headache, fibromyalgia, tinnitus, autism) who receive VNS, the evidence includes case series. Relevant outcomes are symptoms, change in disease status, and functional outcomes. Case series are insufficient to draw conclusions regarding efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

TRANSCUTANEOUS VAGUS NERVE STIMULATION

For individuals with episodic cluster headaches who receive transcutaneous VNS, the evidence includes three RCTs. One RCT for a cluster headache showed a reduction in headache frequency but did not include a sham treatment group. Two randomized, double-blind, sham-controlled studies showed efficacy of achieving pain-free status within 15 minutes of treatment with noninvasive VNS in patients with episodic cluster headaches but not in patients with chronic cluster headaches. The RCTs for episodic cluster headaches are promising, however, additional studies with larger relevant populations are required to establish the treatment efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have other neurologic, psychiatric, or metabolic disorders (e.g., epilepsy, depression, schizophrenia, noncluster headache, impaired glucose tolerance) who receive transcutaneous VNS, the evidence includes RCTs and case series for some of the conditions. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCTs are all small and have various methodologic problems. None showed definitive efficacy of transcutaneous VNS in improving patient outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

POLICY

Vagus nerve stimulation may be considered **medically necessary** as a treatment of medically refractory seizures.

Vagus nerve stimulation is considered **investigational** as a treatment of other conditions, including but not limited to depression, heart failure, upper-limb impairment due to stroke, essential tremor, headaches, fibromyalgia, tinnitus, and traumatic brain injury.

Transcutaneous (nonimplantable) vagus nerve stimulation devices are considered **investigational** for all indications.

POLICY GUIDELINES

Medically refractory seizures are defined as seizures that occur despite therapeutic levels of antiepileptic drugs or seizures that cannot be treated with therapeutic levels of antiepileptic drugs because of intolerable adverse events of these drugs.

Vagal nerve stimulation requires not only the surgical implantation of the device, but also subsequent neurostimulator programming, which occurs intraoperatively and typically during additional outpatient visits.

MEDICARE ADVANTAGE

For Medicare Advantage, the seizures must be medically refractory *partial-onset* seizures for which surgery is not recommended or for which surgery has failed for vagus nerve stimulator to be considered **medically necessary**.

BACKGROUND

VAGUS NERVE STIMULATION

VNS was initially investigated as a treatment alternative in patients with medically refractory partial-onset seizures for whom surgery is not recommended or for whom surgery has failed. Over time, the use of VNS has expanded to include generalized seizures, and it has been investigated for a range of other conditions.

While the mechanisms for the therapeutic effects of VNS are not fully understood, the basic premise of VNS in the treatment of various conditions is that vagal visceral afferents have a diffuse central nervous system projection, and activation of these pathways has a widespread effect on neuronal excitability. An electrical stimulus is applied to axons of the vagus nerve, which have their cell bodies in the nodose and junctional ganglia and synapse on the nucleus of the solitary tract in the brainstem. From the solitary tract nucleus, vagal afferent pathways project to multiple areas of the brain. VNS may also stimulate vagal efferent pathways that innervate the heart, vocal cords, and other laryngeal and pharyngeal muscles, and provide parasympathetic innervation to the gastrointestinal tract.

A type of VNS device addressed in this protocol consists of an implantable, programmable electronic pulse generator that delivers stimulation to the left vagus nerve at the carotid sheath. The pulse generator is connected to the vagus nerve via a bipolar electrical lead. Surgery for implantation of a vagal nerve stimulator involves implantation of the pulse generator in the infraclavicular region and wrapping two spiral electrodes around the left vagus nerve within the carotid sheath. The programmable stimulator may be programmed in advance to stimulate at regular intervals or on demand by patients or family by placing a magnet against the subclavicular implant site.

Various types of devices that transcutaneously stimulate the vagus nerve have been developed as well. The U.S. Food and Drug Administration (FDA) has not approved any transcutaneous VNS devices. Other types of implantable vagus nerve stimulators that are placed in contact with the trunks of the vagus nerve at the gastroesophageal junction are not addressed in this protocol.

Indications

VNS was originally approved for the treatment of medically refractory epilepsy. Significant advances have been made since then in the surgical and medical treatment of epilepsy, and newer, more recently approved medications are available. Despite these advances, however, 25% to 50% of patients with epilepsy experience breakthrough seizures or suffer from debilitating adverse events of antiepileptic drugs. For these patients, VNS therapy has been used as an alternative or adjunct to epilepsy surgery or medications. Based on observations that patients treated with VNS experience improvements in mood, VNS has been evaluated for the treatment of refractory depression. VNS has been investigated for multiple other conditions which may be affected by either the afferent or efferent stimulation of the vagus nerve, including heart failure, headaches, tremor, fibromyalgia, tinnitus, and traumatic brain injury.

REGULATORY STATUS

In 1997, the NeuroCybernetic Prosthesis (NCP®) System (Cyberonics), a VNS device, was approved by the FDA through the premarket approval process for use in conjunction with drugs or surgery "...as an adjunctive treatment of adults and adolescents over 12 years of age with medically refractory partial onset seizures."¹ There have been subsequent expanded approvals. FDA product code: LYF.

In May 2015, a related VNS therapy, AspireSR® (LivaNova), received supplemental premarketing approval from FDA, although the device was recalled in August 2017.² The AspireSR® device detects high heart rates associated with seizures and responds with stimulation. Adjunctive use of the AspireSR® for the treatment of epileptic seizures was indicated for patients over four years of age who suffer from partial-onset seizures that do not respond to antiepileptic medication.

In May 2017, the gammaCore-S® (electroCore), a noninvasive VNS device, was cleared for marketing by the FDA through the 510(k) process (K171306) for the acute treatment of adults with episodic cluster headaches.³ When the device is applied to the side of the neck by the patient, mild electrical stimulation of the vagus nerve is carried to the central nervous system. Each stimulation using gammaCore-S® lasts two minutes. The patient controls the stimulation strength. FDA product codes: PKR, QAK.

Cerbomed (Erlangen, Germany) has developed a transcutaneous VNS (t-VNS®) system that uses a combined stimulation unit and ear electrode to stimulate the auricular branch of the vagus nerve, which supplies the skin over the concha of the ear. Patients self-administer electrical stimulation for several hours a day; no surgical procedure is required. The device received the CE mark in Europe in 2011 but has not been FDA-approved for use in the United States.

Table 1 includes updates on stimulators pertinent to this protocol.

Table 1. FDA-Approved or -Cleared Vagus Nerve Stimulators

Device Name	Manufacturer	Cleared	PMA/510(k)	Indications
NeuroCybernetic Prosthesis (NCP®)	Cyberonics	1997	P970003	Indicated or adjunctive treatment of adults and adolescents 12 years of age or older with medically refractory partial-onset seizures
		2005	P970003/S50	Expanded indication for adjunctive long-term treatment of chronic or recurrent depression for patients 18 years of age or older experiencing a major depressive episode and have not had an adequate response to four or

Device Name	Manufacturer	Cleared	PMA/510(k)	Indications
		2017	P970003/S207	more adequate antidepressant treatments Expanded indicated use as adjunctive therapy for seizures in patients four years of age or older with partial-onset seizures that are refractory to antiepileptic medications
gammaCore®	ElectroCore	2017	K171306	Indicated for acute treatment of pain associated with episodic cluster headache in adults using noninvasive VNS on the side of the neck

FDA: Food and Drug Administration; PMA: premarket approval; VNS: vagus nerve stimulation.

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

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We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

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