Vagus Nerve Stimulation

**Medical Benefit**

**Effective Date:** 01/01/15  
**Next Review Date:** 11/18

**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

---

**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

<table>
<thead>
<tr>
<th>Individuals:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• With seizures refractory to medical treatment</td>
</tr>
</tbody>
</table>

### Interventions

<table>
<thead>
<tr>
<th>Interventions of interest are:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Vagus nerve stimulation</td>
</tr>
</tbody>
</table>

### Comparators

<table>
<thead>
<tr>
<th>Comparators of interest are:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Standard of care</td>
</tr>
</tbody>
</table>

### Outcomes

Relevant outcomes include:

- Symptoms
- Change in disease status
- Functional outcomes

### Summary of Evidence

The evidence for vagus nerve stimulation (VNS) in individuals who have seizures refractory to medical treatment

---

**Description**

Stimulation of the vagus nerve can be performed by means of an implantable stimulator 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 evidence review also addresses devices that stimulate the vagus nerve transcutaneously.

---

**Populations**

<table>
<thead>
<tr>
<th>Individuals:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• With treatment-resistant depression</td>
</tr>
<tr>
<td>• With chronic heart failure</td>
</tr>
<tr>
<td>• With upper-limb impairment due to stroke</td>
</tr>
<tr>
<td>• With essential tremor, obesity, headache, fibromyalgia, or tinnitus</td>
</tr>
<tr>
<td>• With epilepsy, depression, schizophrenia, headache, or impaired glucose tolerance</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interventions of interest are:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Vagus nerve stimulation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Interventions of interest are:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Transcutaneous vagus nerve stimulation</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Comparators of interest are:</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Standard of care</td>
</tr>
</tbody>
</table>

Relevant outcomes include:

- Symptoms
- Change in disease status
- Functional outcomes

---

**Populations**

<table>
<thead>
<tr>
<th>Individuals:</th>
</tr>
</thead>
</table>

---

**Populations**

<table>
<thead>
<tr>
<th>Individuals:</th>
</tr>
</thead>
</table>

---

**Populations**

<table>
<thead>
<tr>
<th>Individuals:</th>
</tr>
</thead>
</table>

---

**Populations**

<table>
<thead>
<tr>
<th>Individuals:</th>
</tr>
</thead>
</table>
includes randomized controlled trials (RCTs) and multiple observational studies. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCTs reported a significant reduction in seizure frequency for patients with partial-onset seizures. The uncontrolled studies have consistently reported large reductions for a broader range of seizure types in both adults and children. The evidence is sufficient to determine qualitatively that the technology results in a meaningful improvement in the net health outcome.

The evidence for VNS in individuals who have treatment-resistant depression includes one RCT and other non-randomized comparative studies and case series. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCT reported only short-term results and found no significant improvement for 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.

The evidence for VNS in individuals who have chronic heart failure or upper-limb impairment due to stroke includes RCTs and case series. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCTs for both conditions did not show significant improvements in the primary outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for VNS in individuals who have essential tremor, obesity, headache, fibromyalgia, or tinnitus includes case series. Relevant outcomes are symptoms, change in disease status, and functional outcomes. Case series are insufficient to make conclusions regarding efficacy. The evidence is insufficient to determine the effects of the technology on health outcomes.

The evidence for transcutaneous VNS stimulation in individuals who have epilepsy, depression, schizophrenia, headache, or impaired glucose tolerance includes at least one RCT 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 shows definitive efficacy of transcutaneous VNS in improving outcomes among patients. 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 heart failure, fibromyalgia, depression, essential tremor, obesity, headaches, tinnitus, and traumatic brain injury.

Nonimplantable vagus nerve stimulation devices are considered **investigational** for all indications.

**Policy Guidelines**

Medically refractory seizures are defined as seizures that occur in spite of therapeutic levels of antiepileptic drugs or seizures that cannot be treated with therapeutic levels of antiepileptic drugs because of intolerable adverse effects 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 refractive 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. Electrical stimulus is applied to axons of the vagus nerve, which have their cell bodies in the nodose and jugular 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. There are also vagal efferent pathways that innervate the heart, vocal cords, and other laryngeal and pharyngeal muscles, and provide parasympathetic innervation to the gastrointestinal tract that may also be stimulated by VNS.

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 stimulate the vagus nerve transcutaneously have been developed as well. One device made by Cerbomed stimulates the auricular branch of the vagus nerve. Some devices used in studies are not well characterized as to the specific manufacturer or type of device used. The U.S. Food and Drug Administration has not approved any transcutaneous VNS devices.

Other types of implantable vagus nerve stimulators are also available. The Maestro® System (EnteroMedics; St. Paul, MN) consists of a subcutaneously implanted pulse generator and electrodes that are placed in contact with the trunks of the vagus nerve at the gastroesophageal junction. These types of stimulators differ in the location of the pulse generator and electrodes and the stimulation programming settings, and are not addressed in this protocol.

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 effects of antiepileptic drugs. For patients such as these, 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 headaches, tremor, obesity, heart failure, fibromyalgia, tinnitus, and traumatic brain injury.
Regulatory Status

In 1997, the NeuroCybernetic Prosthesis (NCP®) System (Cyberonics), a vagus nerve stimulation (VNS) device, was approved by the U.S. Food and Drug Administration (FDA) through the premarket approval (PMA) 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.”

On July 15, 2005, Cyberonics received PMA supplement approval by FDA for the VNS Therapy™ System “…for the adjunctive long-term treatment of chronic or recurrent depression for patients 18 years of age or older who are experiencing a major depressive episode and have not had an adequate response to four or more adequate antidepressant treatments.”

Cerbomed 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. ElectroCore Medical has developed a noninvasive VNS system (gammaCore®) that is currently being investigated for headache; the device has not been FDA approved for use in the United States.

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.

References

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