Medical Policy
Vagus Nerve Stimulation

Effective Date: December, 2005;
Revised [04/08; 03/10; 12/10; 3/12/ 3/14]

Subject: Vagus Nerve Stimulation (VNS)

Overview: Vagus nerve stimulation (VNS) is a therapy in which electrical pulses are delivered to the cervical portion of the vagus nerve by an implanted generator. Electrical signals are transmitted from the pulse generator to the vagus nerve by the lead.

Policy and Coverage Criteria:

NOTE: Prior Authorization NOT required

Harvard Pilgrim Health Care covers VNS for members with medically and surgically refractory seizures.

Harvard Pilgrim Health Care does NOT cover VNS for any other conditions including, but not limited to, depression. It is considered experimental/investigational and unproven.

Exclusions: VNS for conditions other than epilepsy.

Supporting Information:

1. Technology Assessment: Chronic intermittent electrical stimulation of the left vagus nerve was designed to treat medically refractory epilepsy. The NeuroCybernetic Prosthesis (NCP)® System, also called the VNS Therapy™ System (Cyberonics Inc.), is the only device currently available for this type of neuromodulation therapy. VNS Therapy delivers stimulation via a device implanted just under the skin in the left chest area. The pacemaker-like device sends mild, intermittent electrical impulses through a lead to the left vagus nerve, which then sends signals to the brain. Each device is programmed for the individual patient, and the patient or a caregiver has the ability to initiate or abort stimulation with the use of a hand-held magnet.

2. Literature Review:

Epilepsy: Vagus nerve stimulation for the treatment of epilepsy was FDA approved in 1997. Studies have shown that VNS can reduce the severity and shorten the duration of seizures. Englot et al. (2011) published a meta-analysis of VNS efficacy in epilepsy. The analysis included 3 blinded RCTs, 2 non-blinded RCTs, 10 prospective studies, and many retrospective studies. Results showed that after VNS seizure frequency was reduced by an average of 45%, with a 36% reduction in seizures at 3-12 months after surgery and a 51% reduction after more than 1 year of therapy. The last reported follow ups showed seizures were reduced by 50% or more in about 50% of patients. Review also showed that posttraumatic epilepsy and tuberous sclerosis were positive predictors of a favorable outcome. The authors concluded VNS is an effective and relatively safe adjunctive therapy in patients with medically refractory epilepsy not amenable to resection. They note that it is important to recognize complete seizure freedom is rarely achieved with VNS and a quarter of patients do not respond.

Ghaemi et al. (2010) reported long-term outcomes and predictors of seizure freedom for VNS. Patients with VNS were retrospectively reviewed. Results showed 10 patients remained seizure-free for more than 1 year after implantation. Seizures improved in 89 patients but no changes were observed in 45 patients. The authors identified factors that were significant in the univariate analysis: age at implantation, multifocal interictal epileptiform discharges, unilateral interictal epileptiform discharge, cortical dysgenesis, and psychomotor seizure.
Further review found VNS implantation may render patients with some forms of cortical dysgenesis seizure free. Patients with unilateral interictal epileptiform discharges and earlier implantation achieved the most benefit from VNS.

A 2009 report from Shahwan et al. discussed their experience with VNS in children with refractory epilepsy and the effects of VNS in terms of seizure severity. 26 children who underwent VNS were reviewed for a minimum of 18 months. They were evaluated for clinical characteristics, seizure types, seizure frequency, epilepsy syndrome diagnosis and response to VNS in terms of seizure frequency and seizure severity. Review found that 54% of patients responded to VNS with greater than or equal to 50% seizure reduction. Patients with Lennox-Gastaut syndrome and tonic seizures had a higher responder rate; 78%. Status epilepticus episodes were reduced or ceased in the four patients with recurrent SE. Seizure severity, duration and recovery time decreased in all responders. The results led to the authors concluding decreased seizure severity, recovery time, abolition of daytime drop attacks, and reduced hospitalizations due to SE improved patients’ lives over and above the benefit from seizure frequency reduction.

A 2003 report from the Agency for Healthcare Research and Quality (AHRQ) reviewed management of treatment-resistant epilepsy. The evaluation notes as an adjunct intervention, VNS provided reduction in seizure frequency in some patients. Evidence also did not suggest a dramatic effect of VNS on quality of life.

Additional studies have established VNS as a safe and effective treatment for patients with epilepsy refractory to medical and surgical interventions (Wheeler et al. 2011; Colicchio et al. 2010; Mikati et al. 2009; Kabir et al. 2009; Rychilicki et al. 2006; Vonck et al. 2004).

Depression: Peer-reviewed clinical literature does not support vagus nerve stimulation for treatment-resistant depression. While the procedure itself appears safe and well-tolerated by patients, the efficacy of the treatment is not clear. Rigorous studies establishing the efficacy for treatment resistant major depression are lacking (Holtzheimer, 2013).

Overall, study results have been mixed and further long-term evaluations are necessary to provide a clearer picture of appropriate treatment protocol and patient selection. A 2011 research review by AHRQ on non-drug strategies for treatment-resistant depression did not find enough evidence to support the efficacy of VNS for TRD. Mohr et al. published a 2011 review of VNS and deep brain stimulation for the treatment of depression. In their evaluation, they found the data of VNS to be encouraging. However, they not several issues need to be clarified before the therapies are promoted and implemented within the general population. Further controlled studies are needed with higher statistical power. This would help to identify potential responders who would best respond to VNS. Also, the authors call for cost-benefit analyses to assess the true value of the invasive stimulation technologies.

Bajbouj et al. (2010) reported the two year follow up results of patients who had undergone VNS implantation for treatment-resistant depression. The primary outcome measure was improvement from baseline values over time in the scores of the 28-item Hamilton Rating Scale for Depression. Secondary measures were changes in scores on the MADRS, the 30-item Inventory of Depressive Symptoms – Self Report, the CGI-S Scare and the CGI-I Scale. Response was defined a priori as a 50% or greater reduction in the HRSD28 scores compared with the mean score of 2 baseline visits. Secondary outcome response was defined as a reduction of 50% or more in the score compared with baseline for the MADRS or the IDS-SR30. Remission was defined a priori as a score of 10 or lower for the HRSD28 and the MADRS, or 14 or lower for the IDS-SR30. 49 of 74 patients had 24 month results. Results suggest an improvement in depression severity after treatment for 24 months with the addition of VNS to the existing medication regimens in patients with chronic treatment-refractory depression. The percentage of patients who met the response requirements increased continuously with the increasing duration of treatment. 26 out of 49 patients met the criteria for response after 2 years of treatment. However, comparisons with other interventions are difficult because long-term data are unavailable. The authors note the overall reported VNS responses are better than those previously reported in related studies. This study did not have a control group and other anti-depressant treatments were not measured or compared.

A 2008 systematic review and meta-analysis by Daban et al. evaluated the efficacy of VNS used for treatment resistant depression. Of the 18 studies included in the analysis, only one was randomized. Daban et al. found the current evidence to be promising, but experience and the evidence base is limited. Without large, well-designed studies, the efficacy of the VNS for depression cannot be established.

More recently, Grimm and Bajbouj noted the acute and long-term efficacy of vagus nerve stimulation is still under debate (2010). Current evidence does not adequately explain the exact mode of action of VNS and Grimm and Bajbouj suggest further studies are needed.
Corcoran et al. (2006) studied the safety and efficacy of VNS therapy in 11 patients with chronic TRD in an open-label study. Patients were rated on three different rating scales: HRSD, Montgomery-Asberg Depression Rating Scale (MADRS), and Inventory of Depressive Symptomatology-Subjective Rating (IDS-SR). Response was defined as a ≥ 50% decrease in the HRSD from baseline, and remission was defined as an HRSD score < 10. All three measures of depression were statistically reduced at one year when compared to baseline. There was one responder at three months, two at six months, and six (55%) at one year. Three patients (27%) remitted by one year. Severe adverse events included one suicide (a treatment nonresponder), one patient with multiple occurrences of pulmonary emboli, and two patients with vocal cord palsies. The results of this small study show VNS to be relatively safe and effective; however, it is limited by its small sample size and lack of comparison.

Two reports by Rush et al. (2005a, 2005b) did not show conclusive results. Patients were randomized to receive either active or sham VNS. The authors concluded in the first report that while short-term (10 weeks) therapy with VNS was well tolerated, there was no evidence of efficacy in treatment-resistant depression. The second study reported on the 12 month results of the same population of patients. In this report, the sham patients went on to have 12 months of active VNS and the former active patients received an additional 9 months of VNS therapy. Again, results showed the therapy was well-tolerated by patients and some improvements were seen. However, changes in additional antidepressant therapies were allowed, so the true efficacy of the VNS treatment is unknown. Rush et al. suggested long-term comparative studies to establish whether improvement in depression can be linked to the VNS treatment.

3. Benchmarks:

BCBS MA: Vagus nerve stimulation may be MEDICALLY NECESSARY as a treatment of medically refractory seizures.
Vagus nerve stimulation is INVESTIGATIONAL as a treatment of other conditions, including but not limited to heart failure, fibromyalgia, depression, essential tremor, obesity, and headaches.

Anthem BCBS NH: Implantation of a vagus nerve stimulation device is considered medically necessary in an individual with medically and surgically refractory seizures as evidenced by:
- Failure of more than one trial of single or combination antiepileptic medications, as evidenced by persistent seizures or intolerable side effects of drug therapy; and
- Individual has failed or is not a candidate for resective epilepsy surgery.

Electronic analysis of an implanted neurostimulator pulse generator system for vagus nerve stimulation is considered medically necessary when the implantation occurred because the above criteria were met. Investigational and Not Medically Necessary:
Implantation of a vagus nerve stimulation device is considered investigational and not medically necessary as a treatment for all other conditions, including, but not limited to:
- Alzheimer's disease
- Anxiety and mood disorders
- Autism
- Bipolar disorders
- Bulimia
- Cerebral palsy
- Depression
- Essential tremors
- Fibromyalgia
- Headaches (including cluster and migraine headaches)
- Heart failure
- Obesity
- Seizures (that do not meet the above medically necessary criteria)
- Sleep disorders

Electronic analysis of an implanted neurostimulator pulse generator system for vagus nerve stimulation is considered investigational and not medically necessary when the medically necessary criteria for device implantation are not met.
United HealthCare: Vagus nerve stimulation (VNS) is proven for treating epilepsy in persons without a history of left or bilateral cervical vagotomy.

The U.S. Food and Drug Administration (FDA) identifies a history of left or bilateral cervical vagotomy as a contraindication to vagus nerve stimulation.

Vagus nerve stimulation is unproven for treating all other indications, including the following:

- Alzheimer's disease
- Anxiety disorder
- Autism
- Back and neck pain
- Bipolar disorder
- Bulimia
- Cerebral palsy
- Chronic pain syndrome
- Cluster headaches
- Depression
- Fibromyalgia
- Heart failure
- Migraines
- Morbid obesity
- Narcolepsy
- Obsessive-compulsive disorder
- Paralysis agitans
- Sleep disorders
- Tourette's syndrome

Aetna: Aetna considers vagus nerve electrical stimulators medically necessary durable medical equipment (DME) for shortening the duration or reducing the severity of seizures in members with partial onset seizures who remain refractory to optimal anti-epileptic medications and/or surgical intervention, or who have debilitating side effects from anti-epileptic medications. (Note: Electronic analysis of an implanted neurostimulator pulse generator system for vagus nerve stimulation is considered medically necessary when criteria are met).

Aetna considers transcutaneous vagus nerve stimulation experimental and investigational for the treatment of seizures and all other indications (see below) because the effectiveness of this approach has not been established.

Aetna considers vagus nerve electrical stimulators and transcutaneous vagus nerve stimulation experimental and investigational for the treatment of all other indications because its effectiveness for these indications has not been established (not an all inclusive list):

- Addictions
- Anxiety disorders
- Autism
- Bipolar disorders
- Bulimia
- Cerebral palsy
- Chronic headaches
- Cognitive impairment associated with Alzheimer’s disease
- Coma
- Depression
- Essential tremor
- Fibromyalgia
- Heart failure
- Hemicrania continua
• Mood disorders
• Narcolepsy
• Obesity
• Obsessive-compulsive disorder
• Sleep disorder
• Tinnitus
• Tourette's syndrome

http://www.aetna.com/cpb/medical/data/100_199/0191.html

4. Governmental/Regulatory Agencies:

FDA: The NeuroCybernetic Prosthesis® (NCP) System (Cyberonics Inc.), now called VNS Therapy™, was approved in July 1997 for use as an adjunctive therapy to reduce the frequency of seizures in adults and adolescents older than 12 years of age with medically refractory partial-onset seizures (FDA, 2009). Since the original approval, there have been a number of modifications to the device, the instruments used to implant the electrodes and the stimulator, and the software used to control and program the stimulator (FDA, 2009).

On July 15, 2005, the VNS Therapy System received final Premarket Approval by the FDA. The VNS Therapy System is indicated 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.

CMS: Effective for services performed on or after July 1, 1999, VNS is reasonable and necessary for patients with medically refractory partial onset seizures for whom surgery is not recommended or for whom surgery has failed.

Effective for services performed on or after May 4, 2007, VNS is not reasonable and necessary for resistant depression.


Codes:

ID-9 Codes:
296.3-296.36 – Major depressive disorder, recurrent episode
301.12 – Chronic depressive personality disorder
311 – Depressive disorder, not elsewhere classified

CPT:
61885 - Insertion or replacement of cranial neurostimulator pulse generator, 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 2 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
95970: Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude and duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements) simple or complex brain, spinal cord, or peripheral (i.e., cranial nerve, peripheral nerve, autonomic nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming

References:
   https://www.ecri.org/Documents/EPC/Management_of_Treatment-Resistant_Epilepsy.pdf?ecripdf=true
   http://www.ctaf.org/content/assessment/detail/518
   http://www.ctaf.org/content/assessment/detail/518
   http://www.fda.gov/cdrh/PDF/p970003s050b.pdf