BlueCross BlueShield of Alabama

Name of Policy:

Vagus Nerve Stimulation

Policy #: 260
Category: Surgery

Latest Review Date: March 2014
Policy Grade: D

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

Seizures have been defined as paroxysmal disorders of the central nervous system characterized by abnormal cerebral neuronal discharge, with or without loss of consciousness. Seizures have been further sub-classified into those with a generalized onset, beginning throughout the brain, and those with a partial onset, having a discrete focal onset. There are three principal subtypes of partial-onset seizures:

1. Simple partial seizures: These do not involve alteration of consciousness but may have observable motor components or may solely be a subjective sensory or emotional phenomenon.
2. Complex partial seizures: These are partial-onset seizures that involve an alteration of consciousness.
3. Complex partial seizures, secondarily generalized tonic-clonic convulsions: These are partial-onset seizures that progress to involve both sides of the brain and result in a complete loss of consciousness.

In the past ten years there have been significant advances in surgical treatment for epilepsy and in medical treatment of epilepsy with newly developed and approved medications. Despite these advances, however, 25-50% of patients with epilepsy experience breakthrough seizures or suffer from debilitating adverse effects of antiepileptic drugs. Vagus nerve stimulation (VNS) has been 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. 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. While the mechanisms for the antiepileptic effects of vagal nerve stimulation are not fully understood, the basic premise of VNS in the treatment of epilepsy is that vagal visceral afferents have a diffuse central nervous system projection, and activation of these pathways has a widespread effect on neuronal excitability. Surgery for implantation of a vagal nerve stimulator involves wrapping two spiral electrodes around the left vagus nerve within the carotid sheath. The electrodes are connected to an infraclavicular generator pack. The programmable stimulator may be programmed in advance to stimulate at regular times or on demand by patients or family by placing a magnet against the subclavicular implant site. Some of the side effects during stimulation include cough, hoarseness, voice alteration, and shortness of breath. In 1997, the U.S. Food and Drug Administration (FDA) approved a vagus nerve stimulation device called the NeuroCybernetic Prosthesis System (NCP®, Cyberonics, Inc.). The device was approved 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."

It has been reported that VNS in patients with epilepsy is associated with an improvement in mood. There has been research interest in VNS as a treatment of refractory depression. On July 15, 2005, the VNS Therapy System received final PMA approval by the FDA 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."

VNS therapy has also been investigated for use in other conditions such as headaches, ~~and~~ essential tremors, and obesity.

The Cyberonics Company recommends that the device be implanted by physicians who have had specific training in the implantation of this device and monitored by physicians who have had specific training and expertise in managing treatment-resistant depression and the use of this device.

The VNS Therapy System is not recommended in certain types of patients, including those with an imminent risk for suicide; history of psychotic depression, delusional disorder, schizophrenia, or schizoaffective disorder; rapid-cycling type of bipolar disorder; pregnancy; brain injury or prior brain surgery; cardiac arrhythmias; significant respiratory diseases; history of ulcers; history of vasovagal syncope or having only one vagus nerve.

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 electric 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 U.S. Electrocore has developed a noninvasive VNS (gammaCore®) that is currently being investigated for headache; the device does not have FDA approval.

Policy:

Effective for dates of service on or after May 2, 2014:
Vagus Nerve Stimulation (VNS) meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage as a treatment of medically refractory seizures.

Vagus Nerve stimulation (VNS) does not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage as a treatment of other conditions including but not limited to: essential tremor, headaches, depression, obesity, Alzheimer's disease, chronic heart failure, fibromyalgia, tinnitus and traumatic brain injury and is considered **investigational**.

Non-implantable Vagus Nerve stimulation does not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational**

Effective for dates of service on or after April 8, 2010 and prior to May 2, 2014:
Vagus Nerve Stimulation (VNS) meets Blue Cross and Blue Shield of Alabama's medical criteria for coverage as a treatment of medically refractory seizures.

Vagus Nerve stimulation (VNS) does not meet Blue Cross and Blue Shield of Alabama's medical criteria for coverage as a treatment of other conditions including but not limited to: essential tremor, headaches, depression, obesity, Alzheimer's disease, chronic heart failure, fibromyalgia and is considered **investigational**.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

This policy was created in 2000 and updated periodically with literature review. The most recent update covered the period from January 1, 2013, through February 5, 2014.

Treatment of Seizures

The policy regarding treatment of seizures has expanded the indications over time but was originally based, in part, on a 1998 TEC Assessment that offered the following conclusions.

- Published evidence from two large, well-designed multicenter randomized trials involving over 300 patients demonstrates that the use of vagus nerve stimulation (VNS) as an adjunct to optimal use of antiepileptic drugs in the treatment of medically refractory patients with at least six partial-onset seizures/month reduces seizure frequency by approximately 25% after three months of treatment. In patients who achieve an initial reduction in seizure frequency, the beneficial treatment effect appears to be maintained and may increase with time.
- Adverse effects are mild and consist primarily of hoarseness or voice change during "on" periods of stimulation.
- There is limited information about the use of VNS in patients with other types of seizure disorders.

Based on this TEC Assessment, earlier versions of this policy supported the use of VNS for partial-onset seizures for patients older than 12 years of age.

Tecoma and Iragui observed in a 2006 review that, since approval of VNS for partial seizures, a number of case series including patients with generalized seizures have been published. These series report seizure reduction rates similar to or greater than those reported in partial epilepsy and note that "this body of evidence suggests that VNS has broad antiepileptic efficacy." The authors suggest that these results may be particularly important because resective epilepsy surgery is generally not feasible in these patients.

Other reports which have been published since that time are consistent with their observations. In a French study of 50 consecutive refractory adolescents and adults who were not eligible for surgery and 11 of whom had generalized epilepsy, 58% were classified as responders at three years' follow-up. Generalized epilepsy was predictive of a better outcome than partial epilepsy seizures. Seizure reduction of 61% was also reported in a case series of 12 patients with drug-resistant idiopathic generalized epilepsy. Garcia-Navarrete et al evaluated outcomes after 18 months of follow up for a prospectively-followed cohort of 42 patients with medication-resistant

epilepsy who underwent VNS implantation. Subjects' seizure types were heterogeneous, but 52% had generalized epilepsy. Pharmacotherapy was unchanged during the course of the study. Twenty-seven subjects (63%) were described as "responders," defined as having a 50% or greater reduction in seizure frequency compared with the year before VNS implantation. The reduction in seizure frequency was not statistically significantly different between subjects with generalized and focal epilepsy.

Since publication of the 1998 TEC assessment, there has been interest in expanding the use of VNS to younger patients. Several studies have now reported results that support the safety and efficacy of the device in children with refractory seizures. For example, 60 pediatric patients were treated as part of the double-blind clinical trials conducted to support the FDA application. At 18 months, the median reduction in seizure frequency was 50%, similar to the results achieved in adults. Adverse events were also similar to those recently reported in adults, and none resulted in termination of stimulation. Hornig et al reported on a case series of 19 pediatric patients, with observation periods ranging up to 30 months. Overall, 50% of patients had a 50% reduction in seizure frequency. Patwardhan et al reported that among 38 patients aged 11 months to 16 years with medically refractory seizures, both generalized and partial-onset, 29% had a greater than 90% reduction in seizure frequency after VNS implantation, while 39% had 50% to 90% reduction. Healy et al reported that among 16 patients younger than 12 years who underwent VNS implantation at a single center, nine (56%) experienced a reduction in their seizure frequency of 50% or more. Results from an add-on study to a randomized controlled trial (RCT) designed to compare high-output with low-output VNS stimulation among 41 children with medically refractory epilepsy suggest that VNS does not have adverse effects on cognitive or psychosocial outcomes.

Similar to adult studies, pediatric studies suggest that VNS improves seizure frequency in generalized epilepsy syndromes. In a multicenter study of 28 children with refractory seizures, You et al reported that 15 children (53.6%) showed a greater than 50% reduction in seizure frequency and nine (32%) had a greater than 75% reduction, and there were no significant differences when groups were compared by seizure type or etiology. Tecoma and Iragui cite a multicenter retrospective analysis of 50 children with Lennox Gastaut syndrome (LGS) treated with VNS. Median seizure reduction at six months was 88% for tonic seizures and 81% for atypical absence. You et al compared VNS and total corpus callosotomy for LGS. Of the 14 patients who underwent a corpus callosotomy, nine (64%) had a greater than 50% reduction in seizure frequency and five (36%) had a greater than 75% reduction. Of the 10 patients who underwent VNS implantation, seven (70%) had a greater than 50% reduction in seizure frequency and two (20%) had a greater than 75% reduction. For 24 children with LGS or LGS-like syndrome who underwent VNS implantation, Cukiert et al reported that at least a 50% seizure frequency decrease was seen for 35 different seizure types.

The major limitations of VNS are the following issues: stimulation generally does not completely eliminate seizures, and it is not possible to predict which patients will optimally respond. One meta-analysis that included 74 retrospective and prospective studies assessing VNS efficacy in seizures found that predictors of efficacy included generalized epilepsy or mixed seizure types (compared with partial-onset seizures) and age younger than 18 years. In 2013, Arya et al reported results of a single-center retrospective chart review that included 43 pediatric

patients who underwent VNS implantation over a five-year period; the authors found that absence of magnetic resonance imaging lesion predicted a good outcome. These studies support the use of VNS in children, in patients with generalized epilepsy, and in those who are not candidates for surgery (i.e., no identified structural brain abnormality).

The evidence on the efficacy of VNS for treatment of refractory seizures consists of two RCTs and numerous uncontrolled studies. The RCTs both 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 large reduction in seizures includes substantial numbers of patients who achieve a greater than 50% reduction in seizure frequency.

Treatment of Refractory Depression

Interest in the application of VNS for treatment of refractory depression is related to reports of improvement in depressed mood among epileptic patients undergoing VNS. TEC Assessments written in 2005 and updated in 2006 concluded that evidence was insufficient to permit conclusions of the effect of VNS therapy on health outcomes. The available evidence for these TEC Assessments included study groups assembled by the manufacturer of the device (Cyberonics) and have since been reported on in various publications. Analyses from these study groups were presented for U.S. Food and Drug Administration (FDA) review and consisted of a case series of 60 patients receiving VNS (Study D-01), a short-term (i.e., three-month) sham-controlled RCT of 221 patients (Study D-02), and an observational study comparing 205 patients on VNS therapy with 124 patients receiving ongoing treatment for depression (Study D-04). Patients who responded to sham treatment in the short-term RCT (approximately 10%) were excluded from the long-term observational study.

The primary outcome evaluated was the relief of depression symptoms that can usually be assessed by any one of many different depression symptom rating scales. A 50% reduction from baseline score is considered to be a reasonable measure of treatment response. An improvement in depression symptoms may allow reduction of pharmacologic therapy for depression, with a reduction in side effects related to that form of treatment. In the studies evaluating VNS therapy, the 4 most common instruments used were the Hamilton Rating Scale for Depression, Clinical Global Impression, Montgomery and Asberg Depression Rating Scale, and the Inventory of Depressive Symptomatology (IDS).

Several case series studies published before the randomized trial showed rates of improvement, as measured by a 50% improvement in depression score of 31% at 10 weeks to greater than 40% at one to two years, but there are some losses to follow-up. Natural history, placebo effects, and patient and provider expectations make it difficult to infer efficacy from case series data.

The randomized study (D-02) that compared VNS therapy with a sham control (implanted but inactivated VNS) showed a nonstatistically significant result for the principal outcome.(22,23) Fifteen percent of VNS subjects responded versus 10% of control subjects (p=0.31). The Inventory for Depressive Symptomatology Systems Review (IDS-SR) score was considered a secondary outcome and showed a difference in outcome that was statistically significant in favor of VNS (17.4% vs 7.5%, respectively, p=0.04).

The observational study that compared patients participating in the RCT and a separately recruited control group (D-04 vs D-02, respectively) evaluated VNS therapy out to one year and showed a statistically significant difference in the rate of change of depression score. However, issues such as unmeasured differences between patients, non-concurrent controls, differences in sites of care between VNS therapy patients and controls, and differences on concomitant therapy changes raise concern about this observational study. Analyses performed on subsets of patients cared for in the same sites, and censoring observations after treatment changes, generally showed diminished differences in apparent treatment effectiveness of VNS and almost no statistically significant differences. Patient selection for the randomized trial and the observational comparison trial may be of concern. VNS is intended for treatment-refractory depression, but the entry criteria of failure of two drugs and a six-week trial of therapy may not be a strict enough definition of treatment resistance. Treatment-refractory depression should be defined by thorough psychiatric evaluation and comprehensive management. It is important to note that patients with clinically significant suicide risk were excluded from all VNS studies. Given these concerns about the quality of the observational data, these results did not provide strong evidence for the effectiveness of VNS therapy.

In addition to the results of the TEC Assessment, several systematic reviews and meta-analyses have addressed the role of VNS in treatment resistant depression. A systematic review of the literature for VNS of treatment-resistant depression identified the randomized trial previously described among the 18 studies that met the study's inclusion criteria. VNS was found to be associated with a reduction in depressive symptoms in the open studies. However, results from the only double-blind trial were considered to be inconclusive. Daban et al concluded that further clinical trials are needed to confirm efficacy of VNS in treatment-resistant depression.

In a meta-analysis that included 14 studies, Martin and Martin-Sanchez reported that among the uncontrolled studies in their analysis, 31.8% of subjects responded to VNS treatment. However, results from a meta-regression to predict each study's effect size suggested that 84% of the observed variation across studies was explained by baseline depression severity. Berry et al reported results from a meta-analysis of six industry-sponsored studies of safety and efficacy for VNS in treatment-resistant depression, which included the D-01, D-02, Bajbouj et al (D-03), D-04, and Aaronson et al (D-21) study results. In addition, the meta-analysis used data from a registry of patients with treatment-resistant depression (335 patients receiving VNS and treatment as usual and 301 patients receiving treatment as usual) that were unpublished at the time of the meta-analysis publication (online site, ClinicalTrials.gov identifier: NCT00320372). The authors report that adjunctive VNS was associated with a greater likelihood of treatment response (odds ratio, 3.19; 95% confidence interval [CI], 2.12 to 4.66). However, the meta-analysis did not have systematic study selection criteria, limiting the conclusions that can be drawn from it.

In 2013, Aaronson et al reported results from an active-controlled trial in which 331 patients with a history of chronic or recurrent bipolar disorder or major depressive disorder, with a current diagnosis of a major depressive episode, were randomized to one of three VNS current doses (high, medium, low). Patients had a history of failure to respond to at least four adequate dose/duration of antidepressant treatment trials from at least two different treatment categories.

After 22 weeks, the current dose could be adjusted in any of the groups. At follow-up visits at weeks 10, 14, 18, and 22 after enrollment, there was no statistically significant difference between the dose groups for the study's primary outcome, change in IDS score from baseline. However, the mean IDS score improved significantly for each of the groups from baseline to the 22-week follow-up. At 50 weeks of follow-up, there were no significant differences between the treatment dose groups for any of the depression scores used. Most patients completed the study; however, there was a high rate of reported adverse events, including voice alteration in 72.2%, dyspnea in 32.3%, and pain in 31.7%. Interpretation of the IDS improvement over time is limited by the lack of a no treatment control group. Approximately 20% of the patients included had a history of bipolar disorder; as such, the results may not be representative of most patients with treatment resistant unipolar depression.

Other case series do not substantially strengthen the evidence supporting VNS. A case series study by Bajbouj et al that followed patients for two years showed that 53.1% (26/49) patients met criteria for a treatment response and 38.9% (19/49) met criteria for remission. A small study of nine patients with rapid-cycling bipolar disorder showed improvements in several depression rating scales over 40 weeks of observation. Another case series by Cristancho et al that followed patients for one year showed that 4/15 responded and 1/15 remitted according to the principal response criteria.

Adverse effects of VNS therapy included voice alteration, headache, neck pain, and cough, which are known from prior experience with VNS therapy for seizures. Regarding specific concerns for depressed patients such as mania, hypomania, suicide, and worsening depression, there does not appear to be a greater risk of these events during VNS therapy.

There is one RCT evaluating the efficacy of VNS for resistant depression. This study reported only short-term results and found no significant improvement for the primary outcome with VNS. Other available studies, which include nonrandomized comparative studies and case series, are limited by relatively small sizes and the potential for bias in selection; the case series are further limited by the lack of a control group .Given the limitations of this literature, combined with the lack of substantial new clinical trials, the scientific evidence is considered to be insufficient to permit conclusions concerning the effect of this technology on major depression.

Other Conditions

Treatment of Essential Tremor

Handforth et al studied VNS in nine patients with essential tremor. Four weeks after implantation of the VNS device, tremor assessment using a masked videotape of patients was performed. Raters found no improvement in upper-extremity tremors. Therefore, the authors of the study concluded that VNS is not likely to have any clinically meaningful effect in essential tremor treatment.

Treatment of Headaches

Drawing on the analgesic effects noted with VNS in the treatment of depression, Mauskop evaluated VNS in five patients with severe, refractory chronic cluster and migraine headaches. Mauskop reported excellent results in one patient who was able to return to work and significant improvement in two patients. Other than nausea developed by one patient, VNS was well-

tolerated. Cecchini et al evaluated VNS in four patients suffering from daily headache and chronic migraine. However, these studies are too small to draw conclusions on the effects of VNS for the treatment of headache, and further study is needed.

Treatment of Obesity
Unintended weight loss has been observed in participants in studies of VNS, prompting interest in use of the technology to prevent or treat obesity. Bodenlos et al investigated whether VNS might affect food cravings in patients with chronic, treatment-resistant depression. They recruited 33 participants and divided them into three groups; 11 subjects receiving VNS for depression, 11 patients with depression but not receiving VNS, and 11 healthy controls. Most participants (42%) had a body mass index (BMI) in the normal range. Participants viewed food images on a computer in random order and then a second time in the same order and were asked after each viewing how much they would like to eat each food if it were available and how well they would be able to resist tasting each one. VNS devices were turned on for one viewing and off for the other. The depression VNS group had greater differences in food cravings between viewings in the sweet food category than the other two groups. No significant differences between groups were found for foods in proteins and vegetables/fruits categories. A significant proportion of the variability in VNS-related changes in cravings for sweet foods was attributed to clinical VNS device settings, depression scores, and BMI. A number of limitations in the study prevent drawing conclusions about the impact of VNS on eating behavior including small study size, selection and lack of randomization, heterogeneity of groups with respect to depression, BMI, and age. Comorbidities including anxiety and medical conditions and drugs that might influence food intake and cravings were not considered. Large, well-designed and executed controlled studies are needed to evaluate the impact of VNS on eating behavior and obesity.

Treatment of Chronic Heart Failure
A case series Phase 2 trial of VNS therapy for chronic heart failure was found. In this study, De Ferrari et al showed improvements in New York Heart Association class quality of life, six-minute walk test, and left ventricular ejection fraction. These case series findings require confirmation in controlled clinical trials. A randomized study of VNS for heart failure is currently recruiting patients, according to ClinicalTrials.gov.

Treatment of Fibromyalgia
Lange et al conducted a phase 1/2 trial of VNS of 14 patients with fibromyalgia. At three months, five patients had attained efficacy criteria based on a composite measure of improvement of fibromyalgia symptoms. At 11 months, eight patients met efficacy criteria. This single-arm trial does not provide sufficient evidence for efficacy of VNS for this indication.

Treatment of Tinnitus
A ten-patient case series by De Ridder et al suggested that VNS may be associated with clinical improvements in patients with tinnitus.

Treatment of Traumatic Brain Injury
Shi et al have FDA approval to conduct a small pilot study to evaluate VNS in the treatment of traumatic brain injury.

Non implantable VNSs
Two small case series were identified that used a transcutaneous stimulator (t-VNS device) for treatment of medication refractory seizures. In a small case series of ten patients with treatment resistant epilepsy, Stefan et al reported that three patients withdrew from the study, while five of seven patients reported a reduction in seizure frequency. In another small case series, He et al reported that among 14 pediatric patients with intractable epilepsy who were treated with bilateral t-VNS stimulation, of the 13 patients who completed follow-up, mean reduction in self-reported seizure frequency was 31.8% after eight weeks, 54.1% from week nine to 16, and 54.2% from week 17 to 24.

Summary
For patients with refractory seizures, evidence from randomized controlled trials and multiple observational studies supports a reduction in seizure frequency following vagus nerve stimulation (VNS). A TEC Assessment concluded that the evidence is sufficient to permit conclusions on the efficacy of this technique for treatment of refractory seizures. Therefore, VNS may be considered medically necessary for patients with refractory seizures.

For patients with depression, there is some evidence supporting improvements in depressive symptoms after VNS. However, there are a number of limitations of these data, including uncertain clinical significance, lack of evidence on durability, and lack of comparison with alternative treatments. As a result, it is not clear if VNS is as effective as alternatives for specific populations of patients with depression, and VNS is considered investigational for this indication.

For other conditions, including but not limited to headaches, obesity, essential tremor, heart failure, fibromyalgia, tinnitus, and traumatic brain injury, the evidence is limited and not sufficient to permit conclusions on efficacy. VNS is considered investigational for these indications.

The evidence is insufficient to allow conclusions on the efficacy of transcutaneous VNS, and there are no transcutaneous stimulation devices that have FDA approval; therefore, transcutaneous VNS is considered investigational.

Practice Guidelines and Position Statements
In 1999, the American Academy of Neurology (AAN) released a consensus statement on the use of VNS in adults that stated, “VNS is indicated for adults and adolescents over 12 years of age with medically intractable partial seizures who are not candidates for potentially curative surgical resections, such as lesionectomies or mesial temporal lobectomies.” The AAN released an update to these guidelines in 2013 that stated, “VNS may be considered for seizures in children, for LGS [Lennox-Gastaut-syndrome]-associated seizures, and for improving mood in adults with epilepsy (Level C). VNS may be considered to have improved efficacy over time (Level C).”

The American Psychiatric Association guidelines on the treatment of major depressive disorder in adults, updated in November 2010, includes the following statement on the use of VNS: “Vagus nerve stimulation (VNS) may be an additional option for individuals who have not responded to at least four adequate trials of antidepressant treatment, including ECT

[Electroconvulsive therapy]," with a level of evidence III (May be recommended on the basis of individual circumstances).

Key Words:

Vagus nerve stimulation (VNS), partial-onset seizures, depression, headaches, essential tremor, Alzheimer's disease, VNS (t-VNS®), VNS(gammaCore®) Non-implantable Vagus Nerve stimulation

Approved by Governing Bodies:

In July 1997, the Food and Drug Administration (FDA) approved the VNS Therapy System to be used for the following indication:
"For use as an adjunctive therapy in reducing the frequency of seizures in adults and adolescents over 12 years of age with medically refractory partial onset seizures."

In July 2005, The FDA also approved the VNS Therapy System to be used for the following indication:

"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."

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
FEP contracts: FEP does not consider investigational if FDA approved. Special benefit consideration may apply. Refer to member's benefit plan.
Pre-certification requirements: Not applicable

Current Coding:

CPT Codes:

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 array; cranial nerve
64568	Incision for implantation of cranial nerve (e.g., vagus nerve) Neurostimulator electrode array and pulse generator

64569 Revision or replacement of cranial nerve (e.g., Vagus nerve) neurostimulator electrode array. Including connection to pulse generator

64570 Removal of cranial nerve (e.g., vagus nerve) Neurostimulator electrode array and pulse generator

95974 Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, ~~and~~ pulse duration, configuration of wave form, battery status, electrode selectability, output modulation, cycling, impedance and patient compliance measurements); complex cranial nerve neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming, with or without nerve interface testing, first hour

95975 ; with intraoperative or subsequent programming each additional 30 minutes after the first hour (list separately in addition to code for primary procedure)

HCPCS:

L8680 Implantable neurostimulator electrode (with any number of contact points), each

L8686 Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension

Previous Coding

64573 Incision for implantation of neurostimulator electrodes; cranial nerve

E0752 Implantable neurostimulator electrode, each

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Policy History:

Medical Policy Group, March 2006 **(3)**
Medical Policy Administration Committee, March 2006
Available for comment March 14-April 27, 2006
Medical Policy Group, September 2006 **(1)**
Medical Policy Group, October 2007 **(1)**
Medical Policy Group, March 2009 **(4)**
Medical Policy Group, March 2010 **(3)**
Medical Policy Administration Committee, April 2010
Available for comment April 8-May 23, 2010
Medical Policy Group, December 2010 – code updates
Medical Policy Group, March 2011 **(3):** Description, Policy, Key Points, References updated
Medical Policy Group, December 2011 **(3):** 2012 Code Updates – verbiage change to codes 64553. 95974 & 95975
Medical Policy Group, March 2012 **(3):** 2012 Update – Key Points & References
Medical Policy Panel, March 2013
Medical Policy Group, April 2013 **(3):** 2013 Updates to Key Points; no change in policy statement
Medical Policy Panel March 2014

Medical Policy Group March 2014 **(4):** Updated Description, updated policy section by adding that VNS for tinnitus and traumatic brain injury also added non-implantable vagus nerve stimulation devices are investigational. Reworked Key Points Updated Key Words and References.
Available for comment May 2 through July 5, 2014
Medical Policy Group, May 2014 **(5):** 2014 Coding Update: Deleted code L8680 effective July 1, 2014.
Medical Policy Group, June 2014 **(5):** Quarterly 2014 Coding Update: Code L8680 did not delete; Removed delete date and moved code up under active codes.
