

## Medical Policy



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Association

### Title: Vagus Nerve Stimulation

#### Professional

Original Effective Date: June 1, 1997  
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July 1, 1998; January 1, 2006;  
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### 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.

Significant advances have occurred 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.

While the mechanisms for the therapeutic effects of vagal nerve stimulation 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. 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. In 1997, the U.S. Food and Drug Administration (FDA) approved a vagus nerve stimulation device called the NeuroCybernetic Prosthesis (NCP®) system through the Premarket Approval (PMA) process. 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.”

Since 1997, it has been reported that recipients of a vagus nerve stimulator have experienced improvements in mood. Therefore, there has been research interest in VNS as a treatment for refractory depression. On July 15, 2005, Cyberonics received PMA supplement approval by the 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.”

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

## **POLICY**

- A. Vagus nerve stimulation may be considered **medically necessary** as a treatment of medically refractory seizures.
- B. Vagus nerve stimulation is considered **experimental / investigational** as a treatment of other conditions including, but not limited to heart failure, fibromyalgia, depression, essential tremor, obesity, and headaches.

## **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.

## **RATIONALE**

### **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 (1) that offered the following conclusions.

- Published evidence from 2 large, well-designed multicenter trials involving over 300 patients demonstrates that the use of vagus nerve stimulation as an adjunct to optimal use of antiepileptic drugs in the treatment of medically refractory patients with at least 6 partial-onset seizures/month reduces seizure frequency by approximately 25% after 3 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 vagus nerve stimulation in patients with other types of seizure disorders.

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

Since that time, there has been interest in expanding the use of VNS to younger patients. Several studies have now reported results that support the safety of the device in children with refractory seizures. (2) For example, 60 pediatric patients were treated as part of the double-blind clinical trials conducted to support the FDA application. (3) 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, (4) and none resulted in termination of stimulation. Hornig and colleagues reported on a case series of 19 pediatric patients, with observation periods ranging up to 30 months. (5) Overall, 50% of patients had a 50% reduction in seizure frequency. Patwardhan and colleagues reported that among 38 patients aged 11 months to 16 years, 29% had a greater than 90% reduction in seizure frequency, while 39% had 50% to 90% reduction. (6) The major limitations of VNS are the facts that stimulation generally does not completely eliminate seizures, and it is not possible to predict which patients will optimally respond. Therefore, some authors suggest that VNS may be most appropriately used in patients with refractory seizures who are not candidates for surgery (i.e., bilateral or unresectable foci or no identified structural abnormality).

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.” (7) The authors suggest that these results may be particularly important since resective epilepsy surgery is generally not feasible in these patients. More recent reports 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 3 years’ follow-up. (8) Generalized epilepsy was predictive of a better outcome than partial epilepsy seizures. The authors concluded that VNS was a useful palliative procedure in severe generalized epilepsies with atonic or tonic-clonic seizures resulting in frequent falls and entails less risk than callosotomy. 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 9 (32%) had a greater than 75% reduction, and there were no significant differences when groups were compared by seizure type or etiology. (9) Tecoma and Iraqui cite a multicenter retrospective analysis of 50 children with Lennox Gastaut syndrome (LGS) treated with VNS. (7) Median seizure reduction at 6 months was 88% for tonic seizures and 81% for atypical absence. You et al. compared VNS and total corpus callosotomy for LGS. (10) Of the 14 patients who underwent a corpus callosotomy, 9 (64%) had a greater than 50% reduction in seizure frequency and 5 (36%) had a greater than 75% reduction. Of the 10 patients who underwent VNS implantation, 7 (70%) had a greater than 50% reduction in seizure frequency and 2 (20%) had a greater than 75% reduction. Seizure reduction of 61% was also reported in a case series of 12 patients with drug-resistant idiopathic generalized epilepsy. (11) Based on these data, one can conclude that VNS is an effective treatment for refractory seizures other than partial epilepsy.

### **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. (12) However, studies examining VNS for the treatment of depression are limited, and all published and unpublished data concerning clinical outcomes of VNS therapy for the indication of treatment-resistant depression come from company-sponsored clinical studies.

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. (13,14) 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. (15,16) 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., 3-month) randomized sham-controlled clinical trial of 221 patients (Study D-02), and an observational study comparing 205 patients on VNS therapy to 124 patients receiving ongoing treatment for depression (Study D-04). (17) Patients who responded to sham treatment in the short-term randomized, controlled trial (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 1 to 2 years, but there are some losses to follow-up. (18-20) 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 to a sham control (implanted but inactivated VNS) showed a non-statistically significant result for the principal outcome. (15,17) 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 1 year and showed a statistically significant difference in the rate of change of depression score. (16,17) However, issues such as unmeasured differences between patients, nonconcurrent 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. (17) Given these concerns about the quality of the observational data, these results did not provide strong evidence for the effectiveness of VNS therapy.

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. (17)

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 2 drugs and a 6-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.

Data from the case series and clinical trials have been reanalyzed in subsequent publications to show what proportions of patients who respond at one time are still responders at a subsequent time point. Among those who achieved a response at 3 or 12 months, 60–75% of such patients were judged to remain a responder after 1 year. However, this information by itself does not provide evidence of the efficacy of VNS beyond that provided by the original comparative trials. Overall, the available scientific evidence does not demonstrate efficacy of VNS for treatment-resistant depression.

A systematic review of the literature for VNS of treatment-resistant depression identified the randomized trial described above among the 18 studies that met the study's inclusion criteria. (21) VNS was found to be associated with a reduction in depressive symptoms in the open studies. For example, a preliminary report from an ongoing European multicenter open-label efficacy and safety study of VNS for treatment-resistant depression described 1 responder (of 11) at 3 months, 2 responders at 6 months, and 6 responders (55%) at 1 year; 3 patients (27%) were considered to be in remission. (22) However, results from the only double-blind trial were considered to be inconclusive. (15,17) Daban et al. concluded that further clinical trials are needed to confirm efficacy of VNS in treatment-resistant depression. Ongoing studies

include an industry-sponsored dose-comparison study of VNS and a registry for patients with treatment-resistant depression. (23)

A review by Fitzgerald and Daskalakis states that “given the invasive nature of vagal nerve stimulation and potential side effects, further research is urgently required.” (24) A guideline statement from the Canadian Network for Mood and Anxiety Treatments included a review of the literature on VNS for depression in 2009 and concluded that there is a lack of substantial evidence for short-term and long-term efficacy in acute severe depression and that the appropriate place of VNS remains to be determined. (25)

Other case review reports identified do not substantially strengthen the evidence supporting VNS. A case series study by Bajbouj et al. that followed patients for 2 years showed that 53.1% (26/49) patients met criteria for a treatment response and 38.9% (19/49) met criteria for remission. (26) A small study of 9 patients with rapid-cycling bipolar disorder showed improvements in several depression rating scales over 40 weeks of observation. (27) 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. (28)

Given the limitations of prior literature as described in the 2006 TEC Assessment, 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 and colleagues studied VNS in 9 patients with essential tremor. (29) 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 5 patients with severe, refractory chronic cluster and migraine headaches. (30) Mauskop reported excellent results in 1 patient who was able to return to work and significant improvement in 2 patients. Other than nausea developed by 1 patient, VNS was well-tolerated. Cecchini et al. evaluated VNS in 4 patients suffering from daily headache and chronic migraine. (31) 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. (32) They recruited 33 participants and divided them into 3 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 2 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 II trial of VNS therapy for chronic heart failure was found. (33) In this study, De Ferrari et al. showed improvements in New York Heart Association (NYHA) class quality of life, 6-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](http://clinicaltrials.gov).

#### *Treatment of Fibromyalgia*

Lange et al. conducted a Phase I/II trial of VNS of 14 patients with fibromyalgia. (34) At 3 months, 5 patients had attained efficacy criteria based on a composite measure of improvement of fibromyalgia symptoms. At 11 months, 8 patients met efficacy criteria. This single arm trial does not provide sufficient evidence for efficacy of VNS for this indication.

### **Summary**

For patients with refractory seizures, RCT evidence supports a reduction in seizure frequency following vagus nerve stimulation. A TEC Assessment concluded that the evidence is sufficient to permit conclusions on the efficacy of this technique for treatment of refractory seizures. Therefore, vagus nerve stimulation may be considered medically necessary for patients with refractory seizures.

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

For other conditions, including headaches, obesity, essential tremor, heart failure, and fibromyalgia, the evidence is limited and not sufficient to permit conclusions on efficacy. Vagus nerve stimulation is considered investigational for these indications.

**CODING**

**The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

CPT/HCPCS

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 2 or more electrode arrays
64553	Percutaneous implantation of neurostimulator electrode array; 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
95974	Electronic analysis of implanted neurostimulator pulse generator system (eg, rate, pulse amplitude and 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	Electronic analysis of implanted neurostimulator pulse generator system (eg, rate, pulse amplitude and 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, each additional 30 minutes after first hour (List separately in addition to code for primary procedure)
L8680	Implantable neurostimulator electrode, each
L8681	Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
L8685	Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension
L8686	Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension
L8687	Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
L8688	Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension
L8689	External recharging system for battery (internal) for use with implantable neurostimulator, replacement only

- 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. Previously, neurostimulator programming was coded using CPT

codes 63690-63691. In 1999, those codes were deleted, and two new time-based CPT codes were introduced that specifically describe the neurostimulator programming and analysis of cranial nerve stimulation (i.e., vagus nerve) as follows:

- 95974: use modifier 52, if less than 31 minutes in duration

## DIAGNOSIS

345.00-

345.91           Epilepsy, code range

## ICD-10 DIAGNOSES (*Effective October 1, 2014*)

G40.001	Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset, not intractable, with status epilepticus
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
G40.101	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, not intractable, with status epilepticus
G40.109	Localization-related (focal) (partial) symptomatic epilepsy and epileptic syndromes with simple partial seizures, not 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
G40.301	Generalized idiopathic epilepsy and epileptic syndromes, not intractable, with status epilepticus
G40.309	Generalized idiopathic epilepsy and epileptic syndromes, not intractable, without status epilepticus
G40.311	Generalized idiopathic epilepsy and epileptic syndromes, intractable, with status epilepticus
G40.319	Generalized idiopathic epilepsy and epileptic syndromes, intractable, without status epilepticus
G40.401	Other generalized epilepsy and epileptic syndromes, not intractable, with 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
G40.501	Epileptic seizures related to external causes, not intractable, with status epilepticus
G40.509	Epileptic seizures related to external causes, not intractable, without status epilepticus
G40.801	Other epilepsy, not intractable, with status epilepticus
G40.802	Other epilepsy, not intractable, without status epilepticus
G40.811	Lennox-Gastaut syndrome, not intractable, with status epilepticus
G40.812	Lennox-Gastaut syndrome, not intractable, without status epilepticus
G40.813	Lennox-Gastaut syndrome, intractable, with status epilepticus

- G40.814 Lennox-Gastaut syndrome, intractable, without status epilepticus
- G40.821 Epileptic spasms, not intractable, with status epilepticus
- G40.822 Epileptic spasms, not intractable, without status epilepticus
- G40.823 Epileptic spasms, intractable, with status epilepticus
- G40.824 Epileptic spasms, intractable, without status epilepticus
- G40.A01 Absence epileptic syndrome, not intractable, with 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.B01 Juvenile myoclonic epilepsy, not intractable, with status epilepticus
- G40.B09 Juvenile myoclonic epilepsy, not intractable, without status epilepticus
- G40.B11 Juvenile myoclonic epilepsy, intractable, with status epilepticus
- G40.B19 Juvenile myoclonic epilepsy, intractable, without status epilepticus

**REVISIONS**

10-08-2008	Revised title from Vagal Nerve Stimulator to Vagus Nerve Stimulation
	Added Rationale section
	In Coding section: <ul style="list-style-type: none"> <li>▪ Added L8689</li> </ul>
	Added Revisions section
10-26-2010	Description section updated
	In Policy section: <ul style="list-style-type: none"> <li>▪ Policy language liberalized from:                      "Vagal nerve stimulation is medically necessary for:                      1. Patient not responding to anticonvulsant medications with multiple medications tried                      2. Patient not a candidate for a surgical procedure                      3. Medically refractory seizures (i.e. Lennox-Gastaut) in children under 12 years"                      to: "A. Vagus nerve stimulation may be considered medically necessary as a treatment of medically refractory seizures.</li> <li>▪ Policy language liberalized from:                      "Vagal nerve stimulation is experimental / investigational because effectiveness has not been established for all other indications including:                      1. Autism,                      2. Obesity,                      3. Refractory depression,                      4. Obsessive-compulsive disorder,                      5. Cognitive impairment associated with Alzheimer’s disease, and                      6. Depression"                      to: "B. Vagus nerve stimulation is considered experimental / investigational as a treatment of other conditions." with the reference to indications being removed as the list was not all inclusive.</li> </ul>
	Added Policy Guidelines section and the following wording: <ul style="list-style-type: none"> <li>▪ "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."</li> </ul>
	Updated Rationale section

	In Coding section: <ul style="list-style-type: none"> <li>Updated wording for CPT/HCPCS codes: 61886, L8681, L8689</li> </ul> Updated References section
03-03-2011	In Coding section: <ul style="list-style-type: none"> <li>Added CPT codes: 64568, 64569, 64570</li> </ul> Rationale section updated.
	Reference section updated.
01-01-2012	In Coding section: <ul style="list-style-type: none"> <li>Revised CPT nomenclature for the following code: 64553</li> <li>Removed CPT code: 64573</li> <li>Removed the following CPT guidelines: <p>“95974: 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); complex cranial nerve neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming, with or without nerve interface testing, first hour.</p> <p>95975: complex cranial nerve neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming, with or without nerve interface testing, each additional 30 minutes.”</p></li> <li>Added the following CPT guidelines: <p>“95974: use modifier 52, if less than 31 minutes in duration.”</p> </li> </ul>
08-24-2012	Description section updated.
	In the Policy section: <ul style="list-style-type: none"> <li>In Item B, added "including, but not limited to heart failure, fibromyalgia, depression, essential tremor, obesity, and headaches." to read "Vagus nerve stimulation is considered experimental / investigational as a treatment of other conditions, including, but not limited to heart failure, fibromyalgia, depression, essential tremor, obesity, and headaches."</li> </ul>
	Rationale section updated.
	Reference section updated.
06-26-2013	Rational section updated.
	In Coding section: <ul style="list-style-type: none"> <li>Added ICD-10 Diagnoses (<i>Effective October 1, 2014</i>)</li> </ul>

## REFERENCES

1. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Chronic vagus nerve stimulation for treatment of seizures. TEC Assessments 1998; Volume 13, Tab 9.
2. Amar AP, Levy ML, McComb JG et al. Vagus nerve stimulation for control of intractable seizures in childhood. *Pediatr Neurosurg* 2001; 34(4):218-23.
3. Murphy JV. Left vagal nerve stimulation in children with medically refractory epilepsy. The Pediatric VNS Study Group. *J Pediatr* 1999; 134(5):563-6.
4. Morris GL, Mueller WM. Long-term treatment with vagus nerve stimulation in patients with refractory epilepsy. The Vagus Nerve Stimulation Study Group E01-E05. *Neurology* 1999; 53(8):1731-5.
5. Hornig G, Murphy JV, Schallert G et al. Left vagus nerve stimulation in children with refractory epilepsy: an update. *South Med J* 1997; 90(5):484-8.

6. Patwardhan RV, Stong B, Bebin EM et al. Efficacy of vagal nerve stimulation in children with medically refractory epilepsy. *Neurosurgery* 2000; 47(6):1353-8.
7. Tecoma ES, Iragai VJ. Vagus nerve stimulation use and effect in epilepsy: what have we learned? *Epilepsy Behav* 2006; 8(1):127-36.
8. Montavont A, Demarquay G, Ryvlin P et al. Long-term efficiency of vagus nerve stimulation (VNS) in non-surgical refractory epilepsies in adolescents and adults [article in French]. *Rev Neurol (Paris)* 2007; 163(12):1169-77.
9. You SJ, Kang HC, Kim HD et al. Vagus nerve stimulation in intractable childhood epilepsy: a Korean multicenter experience. *J Korean Med Sci* 2007; 22(3):442-5.
10. You SJ, Kang HC, Ko TS et al. Comparison of corpus callosotomy and vagus nerve stimulation in children with Lennox-Gastaut syndrome. *Brain Dev* 2008; 30(3):195-9.
11. Kostov H, Larsson PG, Roste GK. Is vagus nerve stimulation a treatment option for patients with drug-resistant idiopathic generalized epilepsy? *Acta Neurol Scand Suppl* 2007; 187:55-8.
12. Elger H, Hoppe C, Falkai P et al. Vagus nerve stimulation is associated with mood improvements in epilepsy patients. *Epilepsy Res* 2000; 42(2-3):203-10.
13. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Vagus nerve stimulation for treatment-resistant depression. *TEC Assessments* 2005; Volume 20, Tab 8.
14. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Vagus nerve stimulation for treatment-resistant depression. *TEC Assessments* 2006; Volume 21, Tab 7.
15. Rush AJ, Marangell LB, Sackeim HA et al. Vagus nerve stimulation for treatment-resistant depression: a randomized, controlled acute phase trial. *Biol Psychiatry* 2005; 58(5):347-54.
16. George MS, Rush AJ, Marangell LB et al. A one-year comparison of vagus nerve stimulation with treatment as usual for treatment-resistant depression. *Biol Psychiatry* 2005; 58(5):364-73.
17. U.S. Food and Drug Administration Center for Devices and Radiological Health. Summary of Safety and Effectiveness Data for the Vagus Nerve Stimulation (VNS) Therapy System. Available online at: [http://www.fda.gov/ohrms/dockets/ac/04/briefing/4047b1\\_02\\_Summary%20of%20Safety%20and%20Effectiveness.pdf](http://www.fda.gov/ohrms/dockets/ac/04/briefing/4047b1_02_Summary%20of%20Safety%20and%20Effectiveness.pdf). Last accessed January 2011.
18. Rush AJ, George MS, Sackheim HA et al. Vagus nerve stimulation (VNS) for treatment-resistant depression: a multicenter study. *Biol Psychiatry* 2000; 47(4):276-86.
19. Sackeim HA, Rush AJ, George MS et al. Vagus nerve stimulation (VNS) for treatment-resistant depression; efficacy, side effects and predictors of outcome. *Neuropsychopharmacology* 2001; 25(5):713-28.
20. Marangell LB, Rush AJ, George MS et al. Vagus nerve stimulation (VNS) for major depressive episodes: one-year outcomes. *Biol Psychiatry* 2002; 51(4): 280-7.
21. Daban C, Martinez-Aran A, Cruz N et al. Safety and efficacy of vagus nerve stimulation in treatment-resistant depression. A systematic review. *J Affect Disord* 2008; 110(1-2).
22. Corcoran CD, Thomas P, Phillips J et al. Vagus nerve stimulation in chronic treatment-resistant depression: preliminary findings of an open-label study. *Br J Psychiatry* 2006; 189:282-3.
23. Available online at: <http://www.clinicaltrials.gov/>. Last accessed July 2008.
24. Fitzgerald PB, Daskalakis ZJ. The use of repetitive transcranial magnetic stimulation and vagal nerve stimulation in the treatment of depression. *Curr Opin Psychiatry* 2008; 21(1):25-9.

25. Kennedy SH, Milev R, Giacobbe P et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) clinical guidelines for the management of major depressive disorder in adults: IV. Neurostimulation therapies. *J Affect Disord* 2009; 117(suppl 1):S44-53.
26. Bajbouj M, Merkl A, Schlaepfer TE et al. Two-year outcome of vagus nerve stimulation in treatment-resistant depression. *J Clin Psychopharmacol* 2010; 30(3):273-81.
27. Marangell LB, Suppes T, Zboyan HA et al. A 1-year pilot study of vagus nerve stimulation in treatment-resistant rapid-cycling bipolar disorder. *J Clin Psychiatry* 2008; 69(2):183-9.
28. Cristancho P, Cristancho MA, Baltuch GH et al. Effectiveness and safety of vagus nerve stimulation for severe treatment-resistant major depression in clinical practice after FDA approval: outcomes at 1 year. *J Clin Psychiatry* 2011; 72(10):1376-82.
29. Handforth A, Ondo WG, Tatter S et al. Vagus nerve stimulation for essential tremor: a pilot efficacy and safety trial. *Neurology* 2003; 61(10):1401-5.
30. Mauskop A. Vagus nerve stimulation relieves chronic refractory migraine and cluster headaches. *Cephalalgia* 2005; 25(2):82-6.
31. Cecchini AP, Mea E, Tullo V et al. Vagus nerve stimulation in drug-resistant daily chronic migraine with depression: preliminary data. *Neurol Sci* 2009; 30(suppl 1):S101-4.
32. Bodenlos JS, Kose S, Borckardt JJ et al. Vagus nerve stimulation acutely alters food craving in adults with depression. *Appetite* 2007; 48(2):145-53.
33. De Ferrari GM, Crijns HJ, Borggrefe M et al. Chronic vagus nerve stimulation: a new and promising therapeutic approach for chronic heart failure. *Eur Heart J* 2011; 32(7):847-55. Available online at: <http://eurheartj.oxfordjournals.org/content/early/2010/10/28/eurheartj.ehq391.full>. Last accessed January 2011 .
34. Lange G, Janal MN, Maniker A et al. Safety and efficacy of vagus nerve stimulation in fibromyalgia: a phase I/II proof of concept trial. *Pain Med* 2011; 12(9):1406-13

**Other References:**

1. Blue Cross and Blue Shield of Kansas Behavioral Health Liaison Committee, June 2006.
2. Blue Cross and Blue Shield of Kansas Behavioral Health Liaison Committee, June 2007.