

Vagus Nerve Stimulation

Effective: October 1, 2018

Next Review: April 2019

Last Review: September 2018

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Vagus nerve stimulation (VNS) involves implantation of an infraclavicular pulse generator that sends weak electric impulses to the left vagus nerve within the carotid sheath in the neck. This implantable generator is used as a treatment for a number of conditions.

MEDICAL POLICY CRITERIA

Notes:

- This policy does not apply to vagus nerve **blocking** therapy. See cross references.
 - This policy only applies to the initial placement of the device. This policy does not apply to revision(s) or replacement(s) after the device has been placed.
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- I. Vagus nerve stimulation (VNS) may be considered **medically necessary** as a treatment of medically refractory seizures. Patients must have tried and been unresponsive to or intolerant of four antiepileptic drugs.
 - II. VNS is considered **investigational** for all other indications, including but not limited to essential tremors.

III. Non-implantable vagus nerve stimulation devices are considered **investigational** for all indications.

NOTE: A summary of the supporting rationale for the policy criteria is at the end of the policy.

POLICY GUIDELINES

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and Physical/Chart Notes
- Current Symptomology
- Antiepileptic medications given and response

CROSS REFERENCES

1. [Gastric Electrical Stimulation](#); Surgery, Policy No. 111
2. [Vagus Nerve Blocking Therapy for Obesity](#); Surgery, Policy No. 200

BACKGROUND

An implanted VNS device delivers mild electronic impulses via two electrodes connected to the generator and wrapped around the vagus nerve. The stimulator may be programmed in advance or may be activated on demand by placing a magnet against the generator implantation site.

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. Electrical stimulus is applied to axons of the vagus nerve, which have their cell bodies in the nodose and junctional ganglia and synapse on the nucleus of the solitary tract in the brainstem. From the solitary tract nucleus, vagal afferent pathways project to multiple areas of the brain. There are also vagal efferent pathways that innervate the heart, vocal cords, and other laryngeal and pharyngeal muscles, and provide parasympathetic innervation to the gastrointestinal tract that may also be stimulated by VNS.

VNS was originally approved for the treatment of medically-refractory epilepsy. 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% to 50% of patients with epilepsy experience breakthrough seizures or suffer from debilitating adverse effects of antiepileptic drugs. VNS has been used as an alternative to or adjunct to epilepsy surgery or medications as a therapy for refractory seizures.

Based on observations that patients treated with VNS experienced improvements in mood, VNS has been evaluated for the treatment of refractory depression. VNS has been investigated for multiple other conditions which may be affected by either the afferent or efferent stimulation of the vagus nerve, including headaches, tremor, obesity, heart failure, fibromyalgia, tinnitus, and traumatic brain injury.

Recently, less-invasive, non-surgical means of transcutaneous VNS have been developed; however, these non-implantable methods have not yet received approval from the U.S. Food and Drug Administration (FDA) as a treatment for any condition.

REGULATORY STATUS

Implantable VNS Devices

Several VNS therapy systems by Cyberonics Inc. have pre-market approval (PMA) from the U.S. Food and Drug Administration (FDA) for treatment of refractory partial-onset seizures and chronic or recurrent depression, when certain criteria are met. For example, in 1997, the NeuroCybernetic Prosthesis (NCP®) system 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.” The VNS Therapy™ System was approved in 2005 “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.”

Non-implantable VNS Devices

Cerbomed has developed a transcutaneous VNS (t-VNS®) system, NEMOS®, 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 has not been FDA approved for use in the US.

electroCore, LLC has developed a non-invasive VNS (gammaCore®) released for use by the FDA in April of 2017. The device intended for non-invasive vagus nerve stimulation on the side of the neck to treat cluster headache and to reduce the frequency of cluster headache attacks. Product code: PKR

EVIDENCE SUMMARY

VAGUS NERVE STIMULATORS

In order to assess the safety and effectiveness of vagus nerve stimulation (VNS), particularly for indications in which the primary outcomes are subjective (e.g., pain reduction, improved mood, improved functioning), well-designed, randomized controlled trials (RCTs) are necessary. Such trials include double-blinding, appropriate randomization, an appropriate control group (i.e., sham VNS or standard medical treatment), large study populations, adequate follow-up time, and adverse events reporting.

MEDICALLY REFRACTORY SEIZURES

The criteria for VNS for seizures are based on a 1998 BlueCross BlueShield Association (BCBSA) Technology Evaluation Center (TEC) assessment^[1], a 2015 Cochrane review^[2] which included the three published double-blind randomized controlled trials (RCTs)^[3-5], and numerous case series, retrospective reviews, and other non-randomized studies on adult^[6-11], pediatric,^[12-19] or mixed^[20-25] patient populations. Both reviews concluded that VNS reduced seizure frequency in patients with drug resistant partial-onset seizures.

The two RCTs were large, well-designed multicenter trials that reported an approximate 25% reduction in partial-onset seizure frequency following three months of VNS. Adverse effects were mild and consisted primarily of hoarseness or voice change during “on” periods of stimulation. The remaining literature is limited to numerous non-randomized trials. Although evidence from non-randomized studies are generally considered unreliable for assessing the safety and effectiveness of VNS, the findings from these numerous studies have consistently shown significantly reduced seizure activity in patients with drug-resistant epilepsy. In addition, clinical practice guidelines from the American Academy of Neurology stated that “...sufficient evidence exists to rank VNS for epilepsy as effective and safe...”^[26] Thus, despite the lack of RCTs in the published clinical evidence, VNS has become a recognized standard of care for treatment in selected patients with medically refractory seizures.

More recently, a 2014 RCT reported long-term quality of life outcomes for 112 patients with pharmaco-resistant focal seizures, which supported the beneficial effects of VNS for this group.^[27]

REFRACTORY DEPRESSION

Technology Assessments

A 2006 BCBSA TEC Assessment^[28], evaluated the effectiveness of VNS in the treatment of refractory depression compared with continued medical management. The evidence consisted of one case series, one observational study, and one randomized controlled trial. The assessment found that “overall, the evidence supporting efficacy of VNS is not strong.”

The randomized controlled trial (RCT) of 221 patients that compared VNS with a sham control (implanted but inactivated VNS) did not show a statistically significant difference between VNS and continued medical therapy in relieving depression symptoms.^[29-31] The trial was short and possibly underpowered to detect a smaller amount of VNS benefit. In addition, the adequacy of blinding was questionable. The observational study included a subset of 205 VNS treated patients from the RCT described above who were followed long-term. A separately recruited control group of 124 patients received ongoing treatment for depression.^[29,32] Although the study findings favored the VNS therapy group, this evidence is considered unreliable due to significant methodological limitations including but not limited to the following: 1) Non-randomized allocation of treatment does not control for possible between-group differences in individual patient characteristics; thus, it cannot be ruled out that these differences, rather than the treatments received, were responsible for the observed outcomes; 2) The lack of a sham study group does not control for the expected placebo effects; 3) The inadequate, non-concurrent comparison group does not permit conclusions on the efficacy of VNS compared with placebo or other treatment options, 4) The differences in sites of care between VNS treated patients and controls may introduce response bias. (Analysis 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.); and 5) Differences in concomitant therapy changes cannot be ruled out as an explanation of the observed outcomes.

The case series (Study D-01) was a feasibility study of 60 patients receiving VNS; improvement was reported in depression scores.^[33] It is uncertain whether loss to follow-up was addressed adequately in the analysis. In addition, the case series is limited by the lack of an appropriate comparison group.

Systematic Reviews

In a meta-analysis that included 14 studies, Martin (2012) reported that among the uncontrolled studies in their analysis, 31.8% of subjects responded to VNS treatment.^[34] 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 ($p < 0.0001$). The authors concluded that current data was insufficient to determine whether VNS is an effective treatment for depression and noted that positive results from uncontrolled studies may be due to placebo effect.

A 2008 systematic review and meta-analysis for VNS of treatment-resistant depression identified no new RCTs since the pivotal RCT described above, which the authors determined to be inconclusive.^[35] As noted above, RCTs are considered the appropriate design for studying VNS for any indication. However, this review also included 17 nonrandomized, open studies which found VNS to be associated with a reduction in depressive symptoms. The authors concluded that, while open studies have reported promising results, further clinical trials are needed to study the mechanism of action and cost-effectiveness, and to confirm the efficacy of VNS in treatment-resistant depression.

Randomized Controlled Trials

Since the BCBSA TEC Assessment and the 2008 systematic review, a single randomized controlled trial was identified that evaluated the effectiveness of VNS for treatment of refractory depression. Aaronson randomized 331 patients with treatment-resistant depression (TRD) into one of three VNS dose groups: LOW (0.25 mA current, 130 μ s pulse width), MEDIUM (0.5-1.0 mA, 250 μ s), or HIGH (1.25-1.5 mA, 250 μ s).^[34] Patients were included that had a history of failure to respond to at least 4 adequate dose/duration of antidepressant treatment trials from at least 2 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, defined as a change in the Inventory of Depressive Symptomatology (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; and therefore, the results may not be representative of most patients with treatment resistant unipolar depression. The lack of a placebo comparison group within this study limits conclusions regarding the isolated treatment effect of VNS in this patient population.

Nonrandomized Studies

Numerous non-randomized studies evaluated the effectiveness of VNS for the treatment of refractory depression.^[33,35-41] It is not possible to reach reliable conclusions from these studies as they fail to control for the biases discussed above.

TREATMENT OF CHRONIC HEART FAILURE

Randomized Controlled Trials

In 2015, Zannad reported results from the NECTAR-HF trial, a randomized, sham-controlled trial to outcomes from VNS in patients with severe left ventricular (LV) dysfunction despite optimal medical therapy.^[42] Ninety-six patients were implanted with VNS and randomized in a 2:1 manner to VNS ON or VNS OFF for 6 months. Programming of the generator was performed by a physician un-blinded to treatment assignment, while all other investigators and site study staff involved in endpoint data collection were blinded to randomization. Sixty-three patients were randomized to the intervention, of whom 59 had paired pre-post data available, while 32 were randomized to control, of whom 28 had paired data available. The analysis was a modified intention-to-treat. For the primary endpoint of change in left ventricular end systolic diameter (LVESD) from baseline to 6 months, there were no significant differences between groups (P=0.60 between-group difference in LVESD change). Other secondary efficacy endpoints related to LV remodeling parameters, LV function, and circulating biomarkers of heart failure, did not differ between groups, with the exception of SF-60 physical component score, which showed greater improvement in the VNS ON group than in the control group (from 36.3 to 41.2 in the VNS ON group vs from 37.7 to 38.4 in the control group; P=0.02). Subject blinding was found to be imperfect, which may have biased the subjective outcome data reporting.

In the ANTHEM-HF study (2014), 60 patients with heart failure with reduced ejection fraction were implanted with VNS, randomly assigned to right- or left-sided implantation (n=29 and 31, respectively), and followed for 6 months.^[43] Overall, from baseline to 6 month follow-up, LV ejection fraction improved by 4.5% (95% CI 2.4 to 6.6), left ventricular end systolic volume (LVESV) improved by -4.1 mL (95% CI -9.0 to 0.8), LVESD improved by -1.7 mm (95% CI -2.8 to -0.7), heart rate variability improved by 17 ms (95% CI 6.5 to 28), and 6-minute walk distance improved by 56 m (95% CI 37 to 75). Given there was no sham comparator group, it is unclear if the observed improvements may be attributed to VNS or some other confounding factor.

Nonrandomized Studies

Several small case series describe VNS treatment outcomes in patients with heart failure; however, for the reasons noted above, evidence from non-randomized studies is considered unreliable in the study of VNS as a treatment for any indication.^[44,45]

OTHER INDICATIONS

Nonrandomized Studies

Small case series (n ≤ 40 patients) and one non-randomized comparison study described experiences with VNS in patients with bulimia, anxiety, Alzheimer's disease^[46,47], migraine headaches^[48,49], obesity, essential tremor^[50], and eating disorders including obesity and food cravings^[51]. The utility of VNS added to behavioral management of autism and autism spectrum disorders has been posited but there are no RCTs. For the reasons noted above, evidence from non-randomized studies is considered unreliable in the study of VNS as a treatment for any indication.

TRANSCUTANEOUS VAGUS NERVE STIMULATORS

Only conditions for which there is at least one RCT will be discussed, as case series are inadequate to determine the effect of the technology.

REFRACTORY EPILEPSY

Aihua (2014) reported results from a series of 60 patients with pharmaco-resistant epilepsy treated with a transcutaneous VNS (t-VNS) device, who were randomly assigned to receive stimulation over the earlobe (control group) or the Ramsay-Hunt zone (treatment group), which includes the external auditory canal and the conchal cavity and is considered to be the somatic sensory territory of the vagus nerve.^[52] Thirty patients were randomized to each group; 4 subjects from the treatment group were excluded from analysis due to loss to follow-up (n=3) or adverse effects (n=1), while 9 subjects from the control group were excluded from analysis due to loss to follow-up (n=2) or increase or lack of decrease in seizures or other reasons (n=7). In the treatment group, compared with baseline, the median monthly seizure frequency was significantly reduced after 6 months (5.5 vs 6.0; $p<0.001$) and 12 months (4.0 vs 6.0; $p<0.001$) of t-VNS therapy. At 12-month follow-up, t-VNS group subjects had a significantly lower median monthly seizure frequency compared with the control group (4.0 vs 8.0; $p<0.001$).

Two small case series were identified that used a t-VNS device for treatment of medication-refractory seizures. In a small case series of 10 patients with treatment-resistant epilepsy, Stefan (2012) reported that 3 patients withdrew from the study, while 5 of 7 patients reported a reduction in seizure frequency.^[53] In another small case series, He (2013) reported that among 14 pediatric patients with intractable epilepsy who were treated with bilateral t-VNS, of the 13 patients who completed follow-up, mean reduction in self-reported seizure frequency was 31.8% after 8 weeks, 54.1% from week 9 to 16, and 54.2% from week 17 to 24.^[54]

PSYCHIATRIC DISORDERS

Hein (2013) reported results of two pilot RCTs of a t-VNS device for the treatment of depression, one which included 22 subjects and the other with 15 subjects.^[55] In the first study, 11 subjects each were randomized to active or sham t-VNS. At 2 weeks follow-up, Beck Depression Inventory (BDI) self-rating scores in the active-stimulation group decreased from 27.0 to 14.0 points ($p<0.001$), while the sham-stimulated patients did not show significant reductions in the BDI (31.0 to 25.8 points). In the second study, seven patients were randomized to active t-VNS and eight patients were randomized to sham t-VNS. In this study, BDI self-rating scores in the active stimulation group decreased from 29.4 to 17.4 points ($p<0.05$) after 2 weeks, while the sham-stimulated patients did not show significant change in BDI (28.6 to 25.4 points). The authors do not report direct comparisons in BDI change between the sham- and active-stimulation groups.

Hasan (2015) reported a randomized trial of t-VNS for the treatment of schizophrenia.^[56] Twenty patients were assigned either to active t-VNS or to sham treatment for 12 weeks. There was no statistically significant difference in the improvement of schizophrenia status during the observation period.

Shiozawa (2014) conducted a systematic review of studies evaluating the evidence related to transcutaneous stimulation of the trigeminal or vagus nerve for psychiatric disorders.^[57] They found four studies that addressed t-VNS for psychiatric disorders and included a total of 84 subjects. Three of the four studies evaluated physiologic parameters in healthy patients and one evaluated pharmaco-resistant epilepsy (Stefan, previously described^[53]). The authors also include a fifth study in a data table, although not in their text or reference list (Hein, previously described^[55]). Overall, the studies included were limited by small size and poor generalizability.

HEADACHE

Goadsby (2014) reported results from an open-label pilot study of t-VNS for the treatment of migraine with or without aura.^[58] Eighty migraine attacks were self-treated by 27 patients, of an initial sample of 30 patients (two patients treated no migraine attacks with the device, one patient treated only an aura). Of 54 moderate or severe attacks treated, 12 subjects (22%) were pain-free at two hours posttreatment. Thirteen subjects reported adverse events, which were all considered mild or moderate.

IMPAIRED GLUCOSE TOLERANCE

Huang (2014) reported results of a pilot RCT of a t-VNS device that provides stimulation to the auricle for the treatment of impaired glucose tolerance.^[59] The study included 70 patients with impaired glucose tolerance who were randomized to active or sham t-VNS, along with 30 controls who received no t-VNS treatment. After 12 weeks of treatment, patients who received active t-VNS were reported to have significantly lower 2-hour glucose tolerance test results than those who received sham t-VNS (7.5 mmol/L vs 8 mmol/L; $p=0.004$).

ADVERSE EVENTS

The most commonly reported adverse effects of VNS have been mild and consist primarily of hoarseness of voice during "on" periods of stimulation, transient throat pain, and coughing. More serious adverse events reported include, but are not limited to direct delivery of the current to the nerve due to generator malfunction; modified synchronization between cardiac and respiratory activity affecting the oxygen delivery to tissues; heart block with ventricular standstill; bradyarrhythmias and severe asystolia; and changes in respiration during sleep.^[1,29,35,60-63]

NON-IMPLANTABLE VAGUS NERVE STIMULATORS FOR CLUSTER HEADACHE

The only FDA released device is the gammaCore®, which is intended for non-invasive vagus nerve stimulation (nVNS) on the side of the neck to treat cluster headache and to reduce the frequency of cluster headache attacks.

In 2017, Silberstein reported results from the manufacturer funded ACT1 study – a randomized, double-blind, sham-controlled study of nVNS as a treatment for cluster headache (CH). One hundred fifty subjects were randomized to receive sham control or nVNS treatment for less than or equal to one month; completers could enter a 3-month nVNS open-label phase. A considerable proportion of patients correctly guessed their treatment allocation after their first treatment, though blinding was found to have improved by the end of the one-month period. The primary end point was response rate, defined as the proportion of subjects who achieved pain relief (pain intensity of 0 or 1) at 15 minutes after treatment initiation for the first CH attack without rescue medication use through 60 minutes. Secondary end points included the sustained response rate (15-60 minutes). Subanalyses of episodic cluster headache (eCH) and chronic cluster headache (cCH) cohorts were prespecified.

During the randomized phase of one month, 14 participants discontinued participation from the treatment group, and 8 in the control group discontinued. In the three-month open label period, 17 and 11 discontinued from the treatment and control groups, respectively. Application site reactions and nervous system AEs occurred more frequently with sham treatment than with

nVNS in the double-blind phase. Adverse device effects (ADEs) were reported by 35/150 (nVNS, 11; sham, 24) subjects in the double-blind phase and 18/128 subjects in the open-label phase.

Intent-to-treat analysis included 133 subjects: 60 nVNS-treated (eCH, n = 38; cCH, n = 22) and 73 sham-treated (eCH, n = 47; cCH, n = 26). Authors reported a response in 26.7% of nVNS-treated subjects and 15.1% of sham-treated subjects. Response rates were significantly higher with nVNS than with sham for the eCH cohort (nVNS, 34.2%; sham, 10.6%; $p = 0.008$) but not the cCH cohort (nVNS, 13.6%; sham, 23.1%; $p = 0.48$). Sustained response rates were significantly higher with nVNS for the eCH cohort and total population.

Gaul (2016, 2017) reported the results of the PREVA study - a randomized open-label study of nVNS as a prophylactic therapy for chronic cluster headache (CH) in patients diagnosed at least one year prior to enrollment.^[64,65] The study was funded by the device manufacturer. In a two-week baseline period, all 97 participants received only their individualized standard of care (SoC). Patients were then randomized to a four-week period of SoC with nVNS (n=48) or SoC alone, i.e., control (n=49). Four participants from the SoC with nVNS chose to withdraw; one control participant was removed from the study for failing to meet enrollment criteria. In an optional four-week period following, all participants received SoC with nVNS (n=92); 70 completed the optional period (11 controls discontinued from each group).

Efficacy was evaluated by the mean number of CH attacks per week, defined as the number of attacks during the last two weeks of the randomized phase minus the number of attacks during baseline divided by two. Safety and tolerability were assessed in those who were assigned treatment; and the intent-to-treat (ITT) population was those who had more than one efficacy recording in their home diary after randomization.

In the ITT population (n=45 SoC plus nVNS, n=48 in control) authors reported a mean therapeutic gain of 3.9 fewer CH attacks per week (95% confidence interval (CI): 0.5, 7.2; $p = 0.02$). However, the proportion of participants receiving SoC plus nVNS in the ITT population from the randomized phase with more than 50% response to treatment was 40.0, and in controls who went on to receive treatment in the extension phase, the proportion was 16.7.

During the randomization phase, 38% participants in the SoC plus nVNS group experienced adverse events (AEs), and 27% of controls experienced AEs. In the extension phase, 25% and 24% experienced AEs, respectively. Overall, the most common AEs for any treatment were CH attacks, headache, nasopharyngitis, dizziness, oropharyngeal pain, and neck pain. No serious AEs were considered related to the nVNS device.

The study is limited by a sham placebo control group, which may result in placebo response in the nVNS group.

PRACTICE GUIDELINE SUMMARY

AMERICAN PSYCHIATRIC ASSOCIATION

The American Psychiatric Association (APA) (2010, reaffirmed 2015) has level III* recommendations regarding the use of vagus nerve stimulation (VNS) for patients with major depressive disorder.^[66] Strategies to address nonresponse during an acute phase of depression include VNS as an additional option for individuals who have not responded to at

least four adequate trials of antidepressant treatment, including ECT (electroconvulsive therapy). Maintenance treatment with VNS is also appropriate for individuals whose symptoms have responded to this treatment modality.

* [III] May be recommended on the basis of individual circumstances (As opposed to level I or II which are recommended with substantial and moderate clinical confidence, respectively.)

AMERICAN ACADEMY OF NEUROLOGY

The American Academy of Neurology (AAN) 2013 consensus statement states VNS may be considered for seizures in children, for LGS (Lennox-Gastaut-syndrome)- associated seizures, and for improving mood in adults with epilepsy; and VNS may be considered to have improved efficacy over time.^[67] These statements are based on Level C evidence, which is defined as, “possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population.”

SUMMARY

Although the current evidence is limited, vagus nerve stimulation (VNS) has evolved to a standard of care as a treatment of medically refractory seizures. Therefore, VNS for medically refractory seizures may be considered medically necessary for patients who have had inadequate response to or are intolerant of at least four antiepileptic drugs.

There is not enough research to make conclusions about the benefit of VNS as a treatment for conditions other than medically refractory seizures. Therefore, VNS is considered investigational for all indications other than selected patients with refractory seizures.

There is not enough research to know if transcutaneous vagus nerve stimulation (tVNS) improves health outcomes as a treatment for any condition. In addition, no tVNS devices have received approval from the U.S. Food and Drug Administration (FDA). Therefore, transcutaneous vagus nerve stimulation is considered investigational as a treatment for all indications.

There is not enough research to know if or how well non-invasive vagus nerve stimulation (nVNS) works to treat people with any condition, including but not limited to cluster headache. This does not mean that it does not work, but more research is needed to know. No clinical guidelines based on research recommend nVNS for people with cluster headache or any other condition. Therefore, non-invasive vagus nerve stimulation is considered investigational as a treatment for all indications.

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68. BlueCross BlueShield Association Medical Policy Reference Manual "Vagus Nerve Stimulation." Policy No. 7.01.20

CODES

Codes	Number	Description
CPT	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
	61888	Revision or removal of cranial neurostimulator pulse generator or receiver
	64553	Percutaneous implantation of neurostimulator electrode 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 existing pulse generator
	64570	Removal of cranial nerve (e.g., vagus nerve) neurostimulator electrode array and pulse generator
	95970	Electronic analysis of implanted neurostimulator pulse generator system (eg, rate, pulse amplitude, pulse 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 (ie, cranial nerve, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, without reprogramming
	95971	;simple spinal cord, or peripheral (ie, peripheral nerve, sacral nerve, neuromuscular) neurostimulator pulse generator/transmitter, with intraoperative or subsequent programming
	95974	Electronic analysis of implanted neurostimulator pulse generator system (e.g., rate, pulse amplitude, 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	;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)
	0466T	Insertion of chest wall respiratory sensor electrode or electrode array, including connection to pulse generator (List separately in addition to code for primary procedure)
HCPCS	L8679	Implantable neurostimulator, pulse generator, any type
	L8680	Implantable neurostimulator electrode, each
	L8681	Patient programmer (external) for use with implantable programmable neurostimulator pulse generator, replacement only
	L8682	Implantable neurostimulator radiofrequency receiver
	L8683	Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver
	L8685	Implantable neurostimulator pulse generator, single array, rechargeable, includes extension

Codes	Number	Description
	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

Date of Origin: February 1998