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Subject: Vagus Nerve Stimulation

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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.

Transcutaneous vagus nerve stimulation (tVNS) has been investigated as a non-invasive alternative to surgery for implantable vagus nerve stimulators. tVNS involves stimulation of superficial branches of the vagus nerve on the ear. Investigators have hypothesized that direct stimulation of the afferent nerve fibers on the ear area with afferent vagus nerve distribution may produce an effect similar to VNS with an implanted stimulator.

Vagus nerve blocking therapy for obesity consists of an implantable device that delivers electrical stimulation to branches of the vagus nerve on the anterior abdominal wall. The intent is to intermittently block signals to the intra-abdominal vagus nerve to disrupt hunger sensations and induce feelings of satiety.

Noninvasive vagus nerve stimulation (nVNS) is thought to affect central and peripheral neural circuits that subserve pain and autonomic physiology. The mechanism is not clear, and thus nVNS remains an area of intense investigation.

Summary and Analysis of Evidence: An UpToDate review titled “Vagus nerve stimulation therapy for the treatment of epilepsy” (Schachter, Sirven; 2024) states “(i)n general, vagus nerve stimulation (VNS) therapy is considered a valid treatment option for children and adults with well-documented medically refractory seizures who are opposed to intracranial surgery, are not candidates, or whose medically refractory seizures were not substantially improved by prior intracranial epilepsy surgery. Although there are limited randomized studies in other age groups and seizure types, observational studies reviewed suggest that the benefits of VNS may extend to a broad range of seizure types. The effectiveness of VNS does not appear to vary significantly based on age, neurologic comorbidity, cause

of epilepsy, location of the brain from which seizures arise, or epilepsy syndrome. Identification of factors that accurately predict a clinical response to VNS has been elusive. Although VNS is effective for seizures that originate from any lobe of the brain, one study found that seizures arising from the frontal lobes responded better than seizures arising from the temporal region. Other studies have suggested that VNS may be more effective in patients who have had epilepsy for a shorter period of time and in patients with seizures beginning after one year of age. Earlier age of epilepsy onset is also a predictor of medical intractability. Further studies are needed to identify predictive factors associated with a response to VNS." An UpToDate review titled "Bipolar disorder in adults: Overview of neuromodulation procedures" (Holtzheimer, 2024) states "(i)t is not known if VNS is efficacious as adjunctive treatment for bipolar disorder due to the limited and low quality data that are available." "It is not known whether VNS causes treatment-emergent mania or hypomania in patients with bipolar depression, given the paucity of randomized trials comparing active with sham VNS, and that patients can switch to mania/hypomania in the absence of or despite treatment. In a 10-week randomized trial that included 23 patients with bipolar major depression, one patient receiving active VNS switched to mania. An observational study also reported a case in which a patient with bipolar major depression developed treatment-emergent mania." UpToDate review "Unipolar depression in adults: Overview of neuromodulation procedures" (Holtzheimer, 2024) states " … noninvasive, investigational neuromodulation procedures include … transcutaneous vagus nerve stimulation." An UpToDate review titled "Cluster headache: Treatment and prognosis" (May, 2024)" states "(w)hen chronic cluster headache is unresponsive to medical treatments, various surgical interventions and neurostimulation techniques are potential treatment options, though none are clearly established as effective. In such cases, it is particularly important to exclude potential causes of secondary cluster headache. Neurostimulation techniques, including … vagus nerve stimulation, appear promising but remain investigational." Sant'Anna et al (2021) conducted a systematic review and meta-analysis on clinical trials comparing VNS with medical therapy for the management of chronic heart failure with reduced ejection fraction. Four RCTs and 3 prospective studies were identified (N=1263). Only data from the 4 RCTs were included in the meta-analysis. The certainty of the evidence based on GRADE characteristics was reported as high for all outcomes. The meta-analysis found significant improvements in New York Heart Association (NYHA) functional class, quality of life, 6-minute walk test, and N-terminal-pro brain natriuretic peptide levels in patients treated with VNS compared to sham. The authors acknowledged several limitations, including "(1) small number of studies included, which demonstrate the paucity of RCTs to evaluate the effects of vagal stimulation in this specific population, (2) heterogeneity in the objectives or primary outcomes of each study, and (3) no evidence regarding the etiology of the HF in most of the studies, something we know that may elicit different prognosis." Ramos-Castaneda et al (2022) published a systematic review evaluating VNS on upper limb motor recovery after stroke. Three RCTs by Dawson et al (2021) and Kimberley et al (2019) were pooled for the analysis evaluating the role of implanted VNS. Results demonstrated that implanted VNS improved upper limb motor function based on Fugl-Meyer Assessment-Upper Extremity (FMA-UE) score when compared to control. The authors stated "(t)he systematic review and meta-analysis have some limitations … that include the number of clinical trials was very low and one of the included studies had no comparison group; … a high statistical heterogeneity between studies; … <and> some sources of heterogeneity that could not be evaluated,<e.g.,> the day of primary outcome evaluation, physical rehabilitation protocol parameters, the severity of the lesion, and the vascular region affected by the stroke, among others." VNS has been investigated with small pilot studies or studies evaluating the mechanism of disease for several

conditions, including essential tremor (Marano et al, 2024; Handforth et al, 1998), fibromyalgia (Cai et al, 2024; Lange et al, 2011) and tinnitus (Wu et al, 2024; de Ridder et al, 2014). None of these studies are sufficient to draw conclusions on the effect of VNS on these conditions. Lorupolu et al (2024) reviewed 29 studies of vagus nerve stimulation for treatment of stroke, traumatic brain injury (TBI) and spinal cord injury (SCI); 11 were animal models of stroke, TBI, and SCI, and eight involved humans with stroke. While there was heterogeneity in methods of delivering VNS with respect to rehabilitation therapy in animal studies and human non-invasive studies, a similar methodology was used in all human-invasive VNS studies. In animal studies, pairing VNS with rehabilitation therapy consistently improved motor outcomes compared to controls. Except for one study, all human invasive and non-invasive studies with controls demonstrated a trend toward improvement in motor outcomes compared to sham controls post-intervention. However, compared to non-invasive, invasive VNS studies reported severe adverse events such as vocal cord palsy, dysphagia, surgical site infection, and hoarseness of voice, which were found to be related to surgery. The authors concluded that their review "suggests that VNS (non-invasive or invasive) paired with rehabilitation can improve motor outcomes after stroke in humans. Hence, VNS human studies are needed in people with TBI and SCI. There are risks related to device implantation to deliver invasive VNS compared to non-invasive VNS. Future human comparison studies are required to study and quantify the efficacy vs. risks of paired VNS delivered via different methods with rehabilitation, which would allow patients to make an informed decision." The use of VNS for treatment of rheumatoid arthritis (RA) by various routes has been studied by several groups (Bonaz, B, 2024; Baker et al, 2023; Marsal et al, 2021). Authors believe results are promising, however, clinical efficacy results of fully completed studies are awaited with interest.

POSITION STATEMENT:

Vagus nerve stimulation **meets the definition of medical necessity** as a treatment of medically refractory seizures, defined as seizures that occur despite therapeutic levels of antiepileptic drugs or seizures that cannot be treated with therapeutic levels of antiepileptic drugs, because of intolerable adverse events of these drugs.

The available scientific evidence does not support conclusions regarding the effectiveness of vagus nerve stimulation for all other indications. Vagus nerve stimulation is considered **experimental or investigational** for all other conditions, including but not limited to the following:

- Depression
- Heart failure
- Upper limb impairment due to stroke
- Essential tremor
- Headache
- Fibromyalgia
- Tinnitus
- Traumatic brain injury
- Chronic autoimmune diseases (e.g., rheumatoid arthritis)

Intra-abdominal vagus nerve blocking therapy is considered **experimental or investigational** for all indications, including but not limited to the treatment of obesity. Data in published medical literature are inadequate to permit scientific conclusions on long-term and net health outcomes.

The use of **transcutaneous vagus nerve stimulation (tVNS)** (nonimplantable vagus nerve stimulation device) (e.g., Stivax, GammaCore, and Gammacore Sapphire stimulators) is considered **experimental or investigational** for the treatment of any condition, as there is insufficient clinical evidence to permit conclusions on net health outcomes.

BILLING/CODING INFORMATION:

CPT Coding:

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	Open implantation of cranial nerve (eg, 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
0908T	Open implantation of integrated neurostimulation system, vagus nerve, including analysis and programming, when performed (e.g., SetPoint System) **(investigational)**
0909T	Replacement of integrated neurostimulation system, vagus nerve, including analysis and programming, when performed (e.g., SetPoint System) **(investigational)**
0910T	Removal of integrated neurostimulation system, vagus nerve (e.g., SetPoint System) **(investigational)**
0911T	Electronic analysis of implanted integrated neurostimulation system, vagus nerve; without programming by physician or other qualified health care professional (e.g., SetPoint System) **(investigational)**
0912T	Electronic analysis of implanted integrated neurostimulation system, vagus nerve; with simple programming by physician or other qualified health care professional (e.g., SetPoint System) **(investigational)**

HCPCS Coding:

C1607	Neurostimulator, integrated (implantable), rechargeable with all implantable and external components including charging system (**investigational**)
E0735	Non-invasive vagus nerve stimulator (e.g., gammaCore Sapphire™) (**investigational**)

REIMBURSEMENT INFORMATION:

Refer to sections entitled **POSITION STATEMENT** and **PROGRAM EXCEPTIONS**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage Products: The following National Coverage Determination (NCD) was reviewed on the last guideline reviewed date: VAGUS Nerve Stimulation (VNS) (160.18) located at cms.gov.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request.

DEFINITIONS:

Epilepsy: recurrent, unprovoked paroxysmal transient disturbances of brain function that may be manifested as episodic impairment or loss of consciousness, abnormal motor phenomena, psychic or sensory disturbances, or perturbation of the autonomic nervous system.

Seizure: a transient disturbance of cerebral function due to an abnormal paroxysmal neuronal discharge in the brain.

Vagus nerve (nervus vagus): tenth cranial nerve; supplies sensory fibers to the ear, tongue, pharynx, and larynx, motor fibers to the pharynx, larynx, and esophagus, and parasympathetic and visceral afferent fibers to thoracic and abdominal viscera.

RELATED GUIDELINES:

Gastric Electrical Stimulation, 01-91000-04

OTHER:

None applicable.

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COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy and Coverage Committee on 01/23/25.

GUIDELINE UPDATE INFORMATION:

06/15/00	New Medical Coverage Guideline.
08/23/01	Review of guideline with no revisions.
06/15/02	Revised to delete age limitation.
06/15/03	Review of guideline with no changes in coverage.
06/15/04	Review and revision of guideline; consisting of updated references.
01/01/05	Annual HCPCS update; consisting of the revision of 61885, 61886 and 64590.
04/15/05	Review and revision of guideline; consisting of updated references.
04/15/06	Review and revision of guideline consisting of updated references.
01/01/07	HCPCS coding update consisting of the revision of 64590 and 64595.
06/15/07	Review and revision of guideline consisting of updated references and reformatted guideline.

04/15/08	Review and revision of guideline consisting of updated references.
06/15/09	Scheduled review; no change to position statement. Update references.
01/01/10	Annual HCPCS coding review: revise descriptor for CPT code 61886.
06/15/10	Biennial review; no change in position statement. References updated.
01/01/11	Annual HCPCS coding update. Added codes 64568, 64569 and 64570; deleted code 64573.
01/01/12	Annual HCPCS coding update. Revised 64553, 95974 and 95975 descriptors.
06/15/12	Scheduled review. Revised description section and position statement (added additional indications which are considered experimental/investigational); revised Medicare Advantage program exception and updated references.
01/01/13	Annual CPT coding update. Added codes 0312T, 0313T, 0314T, 0315T, 0316T and 0317T.
06/15/13	Scheduled review. Revised description, position statement and program exceptions section. Updated references and reformatted guideline.
11/15/17	Unscheduled review. Maintained position statement. Revised CPT coding and program exceptions section. Updated references and reformatted guideline.
01/01/18	Annual CPT/HCPCS coding update: revised 64550.
01/01/19	Annual CPT/HCPCS coding update. Deleted 64550, 95974, 95975.
03/15/20	Scheduled review. Revised description and position statement. Updated references.
04/01/21	Quarterly CPT/HCPCS coding update. Added code K1020.
01/01/21	Annual CPT/HCPCS coding update. Revised descriptor 64568.
02/15/22	Scheduled review. Maintained position statement and updated references.
01/01/23	Annual CPT/HCPCS coding update. Deleted 0312T, 0313T, 0314T, 0315T, 0316T, 0317T.
02/15/23	Revision. Updated references and maintained position statement.
05/25/23	Update to Program Exceptions section.
01/01/24	Annual CPT/HCPCS coding update. Added E0735; deleted K1020.
02/15/24	Scheduled review. Revised description, maintain position statements, and updated references.
01/01/25	Annual CPT/HCPCS coding update. Added 0908T, 0909T, 0910T, 0911T, 0912T.
02/15/25	Scheduled review. Revised description and position statement (added autoimmune disease to list of conditions considered E/I). Updated references.
01/01/26	Annual CPT/HCPCS coding update. Added C1607.