

## Clinical Policy: Vagus Nerve Stimulation

Reference Number: CP.MP.12

Date of Last Revision: 07/24

[Coding Implications](#)

[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### Description

Vagus nerve stimulation (VNS) has been used in the treatment of epilepsy and has been studied for the treatment of refractory depression and other indications. Electrical pulses are delivered to the cervical portion of the vagus nerve by an implantable device called a neurocybernetic prosthesis. Chronic intermittent electrical stimulation of the left vagus nerve is designed to treat medically refractory epilepsy.<sup>1</sup> VNS has recently been introduced and approved by the Food and Drug Administration (FDA) as an adjunctive therapy for treatment-resistant major depression.<sup>2</sup>

### Policy/Criteria

- I. It is the policy of health plans affiliated with Centene Corporation® that vagus nerve stimulation (VNS) is **medically necessary** in members/enrollees with medically refractory seizures who meet all of the following:
  - A. Diagnosis of focal onset (formerly partial onset) seizures or generalized onset seizures;
  - B. Intractable epilepsy (both):
    1. Failure of at least one year of adherent therapy of at least two anti-seizure drugs;
    2. Continued seizures which have a major impact on activities of daily living;
  - C. Not a suitable candidate for, is opposed to, or has failed epilepsy surgery;
  - D. Request is for an FDA approved device.
  
- II. It is the policy of health plans affiliated with Centene Corporation that the safety and efficacy of VNS therapy has not been proven for any other conditions, including but not limited to the following:
  - A. Refractory (treatment resistant) major depression or bipolar disorder;
  - B. Headaches;
  - C. Cognitive impairment associated with Alzheimer's disease;
  - D. Addiction;
  - E. Anxiety Disorders;
  - F. Autism;
  - G. Eating Disorders;
  - H. Cancer;
  - I. Crohn's Disease;
  - J. Essential trauma;
  - K. Fibromyalgia;
  - L. Heart failure;
  - M. Impaired glucose tolerance/pre-diabetes;
  - N. Inflammation;
  - O. Overweight and obesity;
  - P. Obsessive-compulsive disorder;
  - Q. Panic disorder;
  - R. Post-traumatic stress disorder;

## CLINICAL POLICY

### Vagus Nerve Stimulation

- S. Prader-Willi Syndrome;
- T. Sjogren's Syndrome;
- U. Rheumatoid arthritis;
- V. Schizophrenia;
- W. Sleep disorders;
- X. Stroke;
- Y. Tinnitus;
- Z. Tourette's syndrome;
- AA. Traumatic brain injury.

- III.** It is the policy of health plans affiliated with Centene Corporation that the current research does not support the use of the following types of VNS therapy over other currently available alternatives, due to the lack of large, high-quality studies supporting their use:
- A. Aspire SR Model 106 (Cyberonics) for VNS;
  - B. Transcutaneous VNS or active auricular transcutaneous electrical nerve stimulation.

### Background

The vagus nerve stimulator is a pacemaker-like device implanted under the skin in the left side of the chest through a small incision, with a second small incision made at the base of the neck.<sup>3</sup> The surgery is performed primarily by a neurosurgeon over approximately 45 to 90 minutes under general anesthesia as an outpatient surgery. There is a small risk of infection, along with additional surgical risks that include inflammation or pain at the incision site, damage to nearby nerves and nerve constriction.<sup>35</sup>

#### *Focal (Partial) Seizures*

Several studies have been done evaluating the safety and efficacy of vagus nerve stimulation (VNS) for treatment of epilepsy. A randomized active-control trial known as the E05 study found that 94 patients (of the total 254 patients in the study) receiving high stimulation showed an average reduction in seizure frequency, compared to baseline, of 28% versus 15% reduction in the 102 patients receiving low stimulation. A total of 310 patients completed the E03 and E05 double-blinded trials. Mean decline of seizure frequency overall was about 25 to 30% compared to baseline. Clinical experience has shown that improvement in seizures is maintained, or may even increase over time, but these data are based on uncontrolled observations. Side effects in both studies were similar and included hoarseness and occasional shortness of breath.<sup>1</sup>

Although questions regarding patient selection criteria, optimal stimulation parameters, and cost-effectiveness in the United States remain under investigation, there is sufficient evidence regarding the benefit and safety of VNS to conclude that VNS may improve health outcomes in patients with medically refractory focal-onset seizures who are not suitable candidates for surgery or in whom surgical treatment has failed.<sup>4</sup>

#### *Generalized seizures*

Study results suggest VNS may be effective for generalized epilepsy. However, case series and observational studies constitute the majority of available evidence. Although VNS is not currently approved by the Food and Drug Administration (FDA) for the treatment of generalized seizures, it is often used in children and other patients and in Europe is approved as adjunct

## CLINICAL POLICY

### Vagus Nerve Stimulation

therapy for epileptic disorders predominantly characterized by generalized or focal seizures that are refractory to antiseizure medications.<sup>1</sup> The National Institute for Health and Care Excellence (NICE) recommends VNS for focal and generalized seizures as an adjunctive therapy in patients who are refractory to antiseizure medications and who are not suitable for resective surgery.<sup>5,6</sup> Additionally, the Scottish Intercollegiate Guidelines Network (SIGN) guidelines recommend VNS for epilepsy in patients unsuitable for resective surgery without stipulating seizure type.<sup>7</sup>

#### *Depression*

VNS was FDA-approved for treatment of resistant depression in 2005. However, VNS has no rigorous research data proving it is efficacious for treatment-resistant, unipolar major depression. Open-label studies suggest VNS may be effective; however, these are at risk for bias due to placebo effects. Two randomized controlled trials (RCTs) of VNS for depression found no benefit, and one of these RCTs had outcomes comparable for active and sham treatment (response rates of 15 versus 10 percent). In addition, there is a lack of thorough safety data for the use of VNS in depression.<sup>2</sup>

#### *Other Investigational Indications*

Ongoing research efforts continue to investigate the role of VNS for the treatment of a variety of indications, including but not limited to cognitive deficits in Alzheimer's disease, resistant obesity, and headaches. Data supporting the long-term safety and efficacy from large clinical trials of VNS for the treatment of these indications, however, continue to be lacking.<sup>13,14,36,37</sup>

#### *AspireSR Model 106 (Cyberonics) for Vagus Nerve Stimulation*

The AspireSR Model 106 (Cyberonics Inc.) received FDA Premarket Approval (PMA) in February 2014. The newest modification to the implantable VNS device detects tachycardia heart rates, which may be associated with an impending seizure, and automatically delivers stimulation to the vagus nerve. Like its predecessors, the AspireSR can also deliver stimulation in the normal and magnet modes. However, when programmed for AutoStim mode, the AspireSR requires no patient interaction to trigger the delivery of electrical stimulation. The AutoStim mode should not be used in patients with significant arrhythmias being treated with pacemakers and/or an implantable defibrillator, beta-blockers, or any other treatment that may impact the intrinsic heart rate.<sup>8,9</sup>

A few small, preliminary studies and case reports have evaluated the AspireSR Model 106, and have shown positive results.<sup>8,9,10</sup> However, there is insufficient evidence to establish the safety and efficacy of the AspireSR Model 106 in reducing seizures until further, high quality trials establish its clinical value.

#### *Transcutaneous (non-implantable) Vagus Nerve Stimulation*

Transcutaneous vagus nerve stimulation (tVNS) has been proposed as a noninvasive alternative to implantable VNS for a variety of indications, including, but not limited to epilepsy, major depression, post-traumatic stress syndrome (PTSD), chronic tinnitus, and headaches. Currently, there are two main ways to apply tVNS. One is to apply stimulation on the ear and the other is cervical noninvasive VNS, superficially applying stimulation in the vicinity of the vagus nerve using a specially designed device, (e.g., gammaCore, Phoenix). Noninvasive auricular tVNS stimulates the afferent auricular branch of the vagus nerve located medial of the tragus at the

entry of the acoustic meatus. Given that the right vagal nerve has efferent fibers to the heart, tVNS is safe to be performed only in the left ear. tVNS has been proposed to study cognitive functioning in patients with epilepsy and major depression. The rationale is that direct stimulation of the afferent nerve fibers on the ear area with afferent vagus nerve distribution should produce a similar effect as classic VNS in reducing depressive symptoms without the burden of surgical intervention. A noninvasive, transcutaneous vagal nerve stimulator has been in use in Europe. In one randomized clinical trial on 47 patients with epilepsy, it was reported that after 24 weeks of daily treatment 16% were seizure free and 38% had reduced seizure frequency.<sup>41</sup> Small studies have shown positive results with tVNS for the treatment of depression.<sup>12,13</sup> Additional, larger, peer-reviewed studies, with longer follow-up are necessary to determine the long-term safety and efficacy of transcutaneous VNS for depression.

gammaCore Sapphire™ (ElectroCore, LLC) is a hand-held prescription device that is placed externally on the side of the neck in the vicinity of the vagus nerve to deliver a low voltage electric signal to the nerve's afferent fibers.<sup>14</sup> gammaCore has received FDA approval for the treatment of both episodic cluster and migraine headaches and more recently for the prevention of cluster headaches (CH). gammaCore is under investigation for the treatment of post-traumatic stress syndrome (PTSD).<sup>38</sup> gammaCore delivers up to 30 stimulations in a 24-hour period, each lasting two minutes. The patient controls the intensity level. Once the maximum daily number of treatments has been reached, the device will not deliver any more treatments until the following 24-hour period. A gammaCore refill card is used to load the device with days of therapy based on a healthcare provider's prescription.<sup>13</sup>

In the randomized PRESTO study, noninvasive vagus nerve stimulation (nVNS.) was superior to sham in the treatment of episodic migraine for pain freedom at 30 minutes and 60 minutes after the first treated attack.<sup>14</sup> In both the ACT1 and ACT2 trials, nVNS was superior to sham therapy in episodic CH but not in chronic CH.<sup>2,14</sup> Another 2020 randomized, double-blind, sham-controlled clinical trial showed when comparing nVNS with sham, no statistically significant differences were found with regards to the primary endpoint of pain freedom at 120 minutes, although differences were found with various secondary endpoints and post hoc analysis.<sup>15</sup>

Preliminary clinical trials of nVNS in various primary headache disorders are encouraging, but, for future studies, it is important to conduct large, properly blinded and controlled trials by independent researchers.<sup>13</sup> Additionally, most studies nVNS devices enrolled participants who did not respond sufficiently to oral drug treatment; thus, the role of neurostimulation in an average population of migraine patients remains unknown.<sup>16</sup>

The Phoenix is a transcutaneous auricular vagus nerve stimulation (tVNS) system in development for the treatment of post-traumatic stress disorder symptoms by delivering electrical stimulation to the pinna of the ear using a proprietary soft silicone conductive earbud connected to a programmable handheld control device. The control software uses an adaptive response algorithm and has multiple treatment modes to allow adjustment of stimulation parameters to customize treatment for individual members. There are no published studies reporting on the use of the Phoenix transcutaneous auricular vagus nerve stimulation (tVNS) system for treatment of PTSD. Published evidence is limited to a preliminary feasibility trial that validated the increase in parasympathetic nerve activity with tVNS during a tilt test and a startle

**CLINICAL POLICY**  
**Vagus Nerve Stimulation**

response test. Results from larger published randomized trials that compare the Phoenix tVNS system to usual care in patients with PTSD are required to demonstrate safety and effectiveness for the treatment of PTSD.<sup>38</sup>

The American Headache Society position statement on integrating new migraine treatments into clinical practice note that empirically validated behavioral treatments with Grade A evidence for the prevention of migraine, including cognitive behavioral therapy, biofeedback, and relaxation therapies, should be considered in the management of migraine. These modalities may also be used alone or in addition to pharmacologic treatment. They note further that several noninvasive devices have been developed and approved by the FDA for the treatment of patients with migraines (i.e., single-pulse transcranial magnetic stimulation, electrical trigeminal nerve stimulation and nVNS).<sup>17</sup> Patients who prefer nondrug therapies, and those who have failed to respond to, have contraindications to, or poor tolerability with pharmacotherapy may be candidates for neuromodulation.<sup>18</sup>

Per UpToDate, “There are several promising but unproven methods using neurostimulation to treat medically refractory cluster headache, including sphenopalatine ganglion stimulation, occipital nerve stimulation, noninvasive VNS, and deep brain stimulation. All are investigational and require further study to confirm long-term benefit and safety.”<sup>14</sup>

*Removal of Implant*

Removal of a vagus nerve stimulator may become necessary due to device malfunction, unbearable side effects, signs of infections, or a lack of efficacy. The device can be turned off in the physician’s office if the patient feels it is not helping or if the patient cannot tolerate the stimulation. If the device needs to be removed, only the pulse generator is removed, as attempting to remove the electrodes from around the nerve can cause damage and is not recommended.<sup>34</sup>

**Coding Implications**

This clinical policy references Current Procedural Terminology (CPT®). CPT® is a registered trademark of the American Medical Association. All CPT codes and descriptions are copyrighted 2023, American Medical Association. All rights reserved. CPT codes and CPT descriptions are from the current manuals and those included herein are not intended to be all-inclusive and are included for informational purposes only. Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

**CPT Codes that Support Coverage Criteria**

<b>CPT® Codes</b>	<b>Description</b>
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

**CLINICAL POLICY**  
**Vagus Nerve Stimulation**

<b>CPT® Codes</b>	<b>Description</b>
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 (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

**HCPCS Codes that Support Coverage Criteria**

<b>HCPCS Codes</b>	<b>Description</b>
C1767	Generator, neurostimulator (implantable), nonrechargeable
C1778	Lead, neurostimulator (implantable)
C1816	Receiver and/or transmitter, neurostimulator (implantable)
C1883	Adaptor/extension, pacing lead or neurostimulator lead (implantable)
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
L8686	Implantable neurostimulator pulse generator, single array, nonrechargeable, includes extension
L8687	Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
L8688	Implantable neurostimulator pulse generator, dual array, nonrechargeable, includes extension
L8689	External recharging system for battery (internal) for use with implantable neurostimulator, replacement only

**HCPCS Codes that Do Not Support Coverage Criteria**

<b>HCPCS Codes</b>	<b>Description</b>
K1020	Noninvasive vagus nerve stimulator

<b>Reviews, Revisions, and Approvals</b>	<b>Revision Date</b>	<b>Approval Date</b>
Deleted age criteria; background updated	09/13	10/13
Reviewed and references and coding updated	09/14	10/14
Combined with VNS for depression policy	10/15	10/15

Reviews, Revisions, and Approvals	Revision Date	Approval Date
Added bipolar disorder to not medically necessary list Converted into new template, added ICD-10 codes		
Updated background with additional information on non-implantable VNS	01/19	
References reviewed and updated. Added CPT code-61888. Added ICD-10 code, G40.311 Specialist review.	07/19	08/19
Added additional investigational indications for VNS to section II. References reviewed and updated. Removed ICD-10 Codes: G40.001, G40.009, G40.201, G40.209, G40.309, G40.A09, G40.409, G40.509, G40.802, G40.909, G40.911 and G40.919. Added ICD-10: G40.813, G40.814.	07/20	08/20
Added new HCPCS code K1020 to a new table of HCPCS codes that do not support coverage criteria. “Experimental/investigational” verbiage replaced with descriptive language in policy statement II and III. Replaced “member” with “member/enrollee.”	04/21	
Annual review. Changed “review date” in the header to “date of last revision” and “date” in the revision log header to “revision date.” Background updated with additional study on nVNS for migraine headaches. References reviewed and updated. Reviewed by specialist.	08/21	08/21
Annual review. Added opposition to surgery as a possibility and removed “resective” in I.C. Additional minor rewording with no clinical significance made in Criteria section. Background updated with no impact on criteria. References reviewed and updated.	08/22	08/22
Annual review completed. Removed II.B. “Obesity”. Additional minor rewording with no clinical significance. Background updated; moved “ <i>Removal of implant</i> ” section to background. ICD-10 Diagnosis code table removed. References reviewed and updated. External specialist reviewed.	08/23	08/23
Annual review. Updated background with no clinical significance. References reviewed and updated.	07/24	07/24

**References**

- Schachter SC. Vagus nerve stimulation therapy for the treatment of epilepsy. UpToDate. [www.uptodate.com](http://www.uptodate.com). Updated January 30, 2024. Accessed June 21, 2024.
- Health Technology Assessment. Vagus nerve stimulation for treatment-resistant depression. Hayes. [www.hayesinc.com](http://www.hayesinc.com). Published February 21, 2019 (annual review January 26, 2022). Accessed June 21, 2024.
- National coverage determination: Vagus nerve stimulation (160.18). Centers for Medicare and Medicaid Services Web site. <https://www.cms.gov/>. Published February 15, 2019. Accessed June 27, 2024.
- Schachter SC. Overview of the management of epilepsy in adults. UpToDate. [www.uptodate.com](http://www.uptodate.com). Updated December 13, 2022. Accessed June 21, 2024.

5. National Institute for Health and Care Excellence. Epilepsies in children, young people and adults — NICE guideline [NG217]. <https://www.nice.org.uk/guidance/ng217/chapter/8-Non-pharmacological-treatments>. Published April 27, 2022. Accessed June 17, 2024.
6. National Institute for Health and Care Excellence. Vagus nerve stimulation for refractory epilepsy in children — Interventional procedures guidance [IPG50]. <https://www.nice.org.uk/guidance/ipg50/chapter/2-The-procedure>. Published March 24, 2004. Accessed June 17, 2024.
7. Scottish Intercollegiate Guidelines Network. Diagnosis and management of epilepsy in adults (SIGN publication no. 143). [https://www.sign.ac.uk/media/1079/sign143\\_2018.pdf](https://www.sign.ac.uk/media/1079/sign143_2018.pdf). Published May 2015. Updated September 2018. Accessed June 17, 2024.
8. Boon P, Vonck K, van Rijckevorsel K, et al. A prospective, multicenter study of cardiac-based seizure detection to activate vagus nerve stimulation. *Seizure*. 2015;32:52 to 61. Doi: 10.1016/j.seizure.2015.08.011
9. Fisher RS, Afra P, Macken M, et al. Automatic Vagus Nerve Stimulation Triggered by Ictal Tachycardia: Clinical Outcomes and Device Performance—The U.S. E-37 Trial. *Neuromodulation*. 2016;19(2):188 to 195. Doi:10.1111/ner.12376
10. Hampel KG, Vatter H, Elger CE, Surges R. Cardiac-based vagus nerve stimulation reduced seizure duration in a patient with refractory epilepsy. *Seizure*. 2015;26:81 to 85. Doi:10.1016/j.seizure.2015.02.004
11. Fang J, Rong P, Hong Y, et al. Transcutaneous Vagus Nerve Stimulation Modulates Default Mode Network in Major Depressive Disorder. *Biol Psychiatry*. 2016;79(4):266 to 273. Doi:10.1016/j.biopsych.2015.03.025
12. Hein E, Nowak M, Kiess O, et al. Auricular transcutaneous electrical nerve stimulation in depressed patients: a randomized controlled pilot study. *J Neural Transm (Vienna)*. 2013;120(5):821 to 827. Doi:10.1007/s00702-012-0908-6
13. Health Technology Assessment. Noninvasive vagus nerve stimulation with gammacore for prevention or treatment of cluster headache. Hayes. [www.hayesinc.com](http://www.hayesinc.com). Published May 12, 2020 (annual review June 7, 2023). Accessed June 21, 2024.
14. May A. Cluster headache: Treatment and prognosis. UpToDate. [www.uptodate.com](http://www.uptodate.com). Updated April 10, 2024. Accessed June 21, 2024.
15. Blech B, Starling AJ, Marks LA, Wingerchuk DM, O’Carroll CB. Is Noninvasive Vagus Nerve Stimulation a Safe and Effective Alternative to Medication for Acute Migraine Control?. *Neurologist*. 2020;25(4):97 to 100. Doi:10.1097/NRL.0000000000000274
16. Evers S. Non-Invasive Neurostimulation Methods for Acute and Preventive Migraine Treatment-A Narrative Review. *J Clin Med*. 2021;10(15):3302. Published 2021 Jul 27. Doi:10.3390/jcm10153302
17. American Headache Society. The American Headache Society Position Statement On Integrating New Migraine Treatments Into Clinical Practice [published correction appears in *Headache*. 2019 Apr;59(4):650 to 651] Doi:10.1111/head.13506. *Headache*. 2019;59(1):1 to 18. Doi:10.1111/head.13456
18. Schwedt TJ, Garza I. Acute treatment of migraine in adults. UpToDate. [www.uptodate.com](http://www.uptodate.com). Updated June 6, 2023. Accessed July 17, 2023.
19. Morris GL 3<sup>rd</sup>, Gloss D, Buchhalter J, Mack KJ, Nickels K, Harden C. Evidence-based guideline update: vagus nerve stimulation for the treatment of epilepsy: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology*. Reaffirmed July 16, 2022. 2013;81(16):1453 to 1459. Doi:10.1212/WNL.0b013e3182a393d1



20. Sirven, JI. Evaluation and management of drug-resistant epilepsy. UpToDate. [www.uptodate.com](http://www.uptodate.com). Updated December 195, 2023. Accessed June 21, 2024.
21. Wilfong A. Seizures and epilepsy in children: Refractory seizures. UpToDate. [www.uptodate.com](http://www.uptodate.com). Updated April 4, 2024. Accessed June 21, 2024.
22. Tassorelli C, Grazzi L, de Tommaso M, et al. Noninvasive vagus nerve stimulation as acute therapy for migraine: The randomized PRESTO study. *Neurology*. 2018;91(4):e364 to e373. Doi:10.1212/WNL.0000000000005857
23. Silberstein SD, Calhoun AH, Lipton RB, et al. Chronic migraine headache prevention with noninvasive vagus nerve stimulation: The EVENT study. *Neurology*. 2016;87(5):529 to 538. Doi:10.1212/WNL.0000000000002918
24. Silberstein SD, Mechtler LL, Kudrow DB, et al. Non-Invasive Vagus Nerve Stimulation for the Acute Treatment of Cluster Headache: Findings From the Randomized, Double-Blind, Sham-Controlled ACT1 Study. *Headache*. 2016;56(8):1317 to 1332. Doi:10.1111/head.12896
25. Goadsby PJ, de Coo IF, Silver N, et al. Non-invasive vagus nerve stimulation for the acute treatment of episodic and chronic cluster headache: A randomized, double-blind, sham-controlled ACT2 study. *Cephalalgia*. 2018;38(5):959 to 969. Doi:10.1177/0333102417744362
26. Klinkenberg S, Aalbers MW, Vles JS, et al. Vagus nerve stimulation in children with intractable epilepsy: a randomized controlled trial. *Dev Med Child Neurol*. 2012;54(9):855 to 861. Doi:10.1111/j.1469-8749.2012.04305.x
27. Holtzheimer PE. Unipolar depression in adults: Treatment with surgical approaches. UpToDate. [www.uptodate.com](http://www.uptodate.com). Updated January 20, 2022. Accessed July 17, 2023.
28. Guan J, Karsy M, Ducis K, Bollo RJ. Surgical strategies for pediatric epilepsy. *Transl Pediatr*. 2016;5(2):55 to 66. Doi:10.21037/tp.2016.03.02
29. Panebianco M, Rigby A, Marson AG. Vagus nerve stimulation for focal seizures. *Cochrane Database Syst Rev*. 2022;7(7):CD002896. Published 2022 Jul 14. Doi:10.1002/14651858.CD002896.pub3
30. Ben-Menachem E, Revesz D, Simon BJ, Silberstein S. Surgically implanted and non-invasive vagus nerve stimulation: a review of efficacy, safety and tolerability. *Eur J Neurol*. 2015;22(9):1260 to 1268. Doi:10.1111/ene.12629
31. Fisher RS, Shafer, PO, D'Souza, C. 2017 Revised Classification of Seizures. Epilepsy Foundation. <https://www.epilepsy.com/article/2016/12/2017-revised-classification-seizures>. Published December 2016. Accessed June 18, 2024.
32. Bauer S, Baier H, Baumgartner C, et al. Transcutaneous Vagus Nerve Stimulation (tVNS) for Treatment of Drug-Resistant Epilepsy: A Randomized, Double-Blind Clinical Trial (cMPsE02). *Brain Stimul*. 2016;9(3):356 to 363. Doi:10.1016/j.brs.2015.11.003
33. Center for Devices and Radiological Health (CDRH). P970003/S50. VNS Therapy System [premarket approval letter]. July 15, 2005. Food and Drug Administration. [https://www.accessdata.fda.gov/cdrh\\_docs/pdf/p970003s050a.pdf](https://www.accessdata.fda.gov/cdrh_docs/pdf/p970003s050a.pdf) Accessed June 18, 2024.
34. Ortler M, Unterhofer C, Dobesberger J, Haberlandt E, Trinkka E. Complete removal of vagus nerve stimulator generator and electrodes. *J Neurosurg Pediatr*. 2010;5(2):191 to 194. Doi:10.3171/2009.9.PEDS0810
35. American Association of Neurological Surgeons (AANS). Vagus nerve stimulation. <https://www.aans.org/en/Patients/Neurosurgical-Conditions-and-Treatments/Vagus-Nerve-Stimulation>. Updated April 9, 2024. Accessed June 20, 2024.

## CLINICAL POLICY

### Vagus Nerve Stimulation

36. Vargas-Caballero M, Warming H, Walker R, Holmes C, Cruickshank G, Patel B. Vagus Nerve Stimulation as a Potential Therapy in Early Alzheimer’s Disease: A Review. *Front Hum Neurosci.* 2022;16:866434. Published 2022 Apr 29. Doi:10.3389/fnhum.2022.866434
37. Pavlov VA. The evolving obesity challenge: targeting the vagus nerve and the inflammatory reflex in the response. *Pharmacol Ther.* 2021;222:107794. Doi:10.1016/j.pharmthera.2020.107794
38. Emerging Technology Report. Phoenix transcutaneous auricular vagus stimulation system (Evren Technologies Inc.) for posttraumatic stress. Hayes. [www.hayesinc.com](http://www.hayesinc.com). Published July 17, 2023. Accessed June 21, 2024.
39. Boluk C, Ozkara C, Isler C, Uzan M. Vagus Nerve Stimulation in Intractable Epilepsy. *Turk Neurosurg.* 2022;32(1):97 to 102. Doi:10.5137/1019-5149.JTN.33775-21.2
40. Hajtovic S, LoPresti MA, Zhang L, Katlowitz KA, Kizek DJ, Lam S. The role of vagus nerve stimulation in genetic etiologies of drug-resistant epilepsy: a meta-analysis. *J Neurosurg Pediatr.* 2022;29(6):667 to 680. Published 2022 Mar 18. Doi:10.3171/2022.1.PEDS222
41. Farmer AD, Strzelczyk A, Finisguerra A, et al. International Consensus Based Review and Recommendations for Minimum Reporting Standards in Research on Transcutaneous Vagus Nerve Stimulation (Version 2020). *Front Hum Neurosci.* 2021;14:568051. Published 2021 Mar 23. doi:10.3389/fnhum.2020.568051

#### **Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan

## CLINICAL POLICY

### Vagus Nerve Stimulation

retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care and are solely responsible for the medical advice and treatment of member/enrollees. This clinical policy is not intended to recommend treatment for member/enrollees. Member/enrollees should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, member/enrollees and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, member/enrollees and their representatives agree to be bound by such terms and conditions by providing services to member/enrollees and/or submitting claims for payment for such services.

**Note: For Medicaid member/enrollees**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

**Note: For Medicare member/enrollees**, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at <http://www.cms.gov> for additional information.

©2016 Centene Corporation. All rights reserved. All materials are exclusively owned by Centene Corporation and are protected by United States copyright law and international copyright law. No part of this publication may be reproduced, copied, modified, distributed, displayed, stored in a retrieval system, transmitted in any form or by any means, or otherwise published without the prior written permission of Centene Corporation. You may not alter or remove any trademark, copyright or other notice contained herein. Centene<sup>®</sup> and Centene Corporation<sup>®</sup> are registered trademarks exclusively owned by Centene Corporation.