



MASSACHUSETTS

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Medical Policy Vagus Nerve Stimulation

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Policy Number: 474

BCBSA Reference Number: 7.01.20 (For Plan internal use only)

Related Policies

- Meniscal Allografts and Other Meniscal Implants, #110
- Spinal Cord and Dorsal Root Ganglion Stimulation, #472
- Responsive Neurostimulation for the Treatment of Refractory Partial Epilepsy, #716
- Transcranial Magnetic Stimulation as a Treatment of Depression, #297
- Deep Brain Stimulation, #473

Policy

Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity

Vagus nerve stimulation may be considered **MEDICALLY NECESSARY** as a treatment of medically refractory seizures.

Vagus nerve stimulation is considered **INVESTIGATIONAL** as a treatment of other conditions, including but not limited to depression, heart failure, upper-limb impairment due to stroke, essential tremor, headaches, fibromyalgia, tinnitus and traumatic brain injury.

Transcutaneous (nonimplantable) vagus nerve stimulation devices are considered **INVESTIGATIONAL** for all indications.

Prior Authorization Information

Inpatient

- For services described in this policy, precertification/preauthorization **IS REQUIRED** if the procedure is performed **inpatient**.

Outpatient

- For services described in this policy, see below for situations where prior authorization **might be required** if the procedure is performed **outpatient**.

	Outpatient
Commercial Managed Care (HMO and POS)	Prior authorization is not required .
Commercial PPO and Indemnity	Prior authorization is not required .

CPT Codes / HCPCS Codes / ICD Codes

Inclusion or exclusion of a code 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 as it applies to an individual member.

Providers should report all services using the most up-to-date industry-standard procedure, revenue, and diagnosis codes, including modifiers where applicable.

The following codes are included below for informational purposes only; this is not an all-inclusive list.

The above medical necessity criteria **MUST be met for the following codes to be covered for Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity:**

CPT Codes

CPT codes:	Code Description
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 electrodes; cranial nerve
64568	Incision for implantation of cranial nerve (eg, vagus nerve) neurostimulator electrode array and pulse generator
95976	Electronic analysis of implanted neurostimulator pulse generator/transmitter (eg, contact group[s], interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with simple cranial nerve neurostimulator pulse generator/transmitter programming by physician or other qualified health care professional
95977	Electronic analysis of implanted neurostimulator pulse generator/transmitter (eg, contact group[s], interleaving, amplitude, pulse width, frequency [Hz], on/off cycling, burst, magnet mode, dose lockout, patient selectable parameters, responsive neurostimulation, detection algorithms, closed loop parameters, and passive parameters) by physician or other qualified health care professional; with complex cranial nerve neurostimulator pulse generator/transmitter programming by physician or other qualified health care professional

The following ICD Diagnosis Codes are considered medically necessary when submitted with the CPT codes above if medical necessity criteria are met:

ICD-10 Diagnosis Codes

ICD-10-CM Diagnosis codes:	Code Description
G40.309	Generalized idiopathic epilepsy and epileptic syndromes, not intractable, without status epilepticus
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
G40.311	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
G40.42	Cyclin-Dependent Kinase-Like 5 Deficiency Disorder
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
G40.803	Other epilepsy, intractable, with status epilepticus
G40.804	Other epilepsy, 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
G40.833	Dravet syndrome, intractable, with status epilepticus
G40.834	Dravet syndrome, intractable, without status epilepticus
G40.841	KCNQ2-related epilepsy, not intractable, with status epilepticus
G40.842	KCNQ2-related epilepsy, not intractable, without status epilepticus
G40.843	KCNQ2-related epilepsy, intractable, with status epilepticus
G40.844	KCNQ2-related epilepsy, intractable, without status epilepticus
G40.89	Other seizures
G40.901	Epilepsy, unspecified, not intractable, with status epilepticus
G40.909	Epilepsy, unspecified, not intractable, without status epilepticus
G40.911	Epilepsy, unspecified, intractable, with status epilepticus

G40.919	Epilepsy, unspecified, 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
G40.C01	Lafora progressive myoclonus epilepsy, not intractable, with status epilepticus
G40.C09	Lafora progressive myoclonus epilepsy, not intractable, without status epilepticus
G40.C11	Lafora progressive myoclonus epilepsy, intractable, with status epilepticus
G40.C19	Lafora progressive myoclonus epilepsy, intractable, without status epilepticus
R56.9	Unspecified convulsions

The following HCPCS code is considered investigational for **Commercial Members: Managed Care (HMO and POS), PPO, Indemnity, Medicare HMO Blue and Medicare PPO Blue:**

HCPCS Codes

HCPCS codes:	Code Description
E0735	Non-invasive vagus nerve stimulator

Description

Vagus nerve stimulation (VNS) was initially 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. Over time, the use of VNS has expanded to include generalized seizures, and it has been investigated for a range of other conditions.

While the mechanisms for the therapeutic effects of VNS 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. An 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. VNS may also stimulate vagal efferent pathways that innervate the heart, vocal cords, and other laryngeal and pharyngeal muscles, and provide parasympathetic innervation to the gastrointestinal tract.

Other types of implantable vagus nerve stimulators that are placed in contact with the trunks of the vagus nerve at the gastroesophageal junction are not addressed in this evidence review.

Summary

Stimulation of the vagus nerve can be performed using a pulsed electrical stimulator implanted within the carotid artery sheath. This technique has been proposed as a treatment for refractory seizures, depression, and other disorders. There are also devices available that are implanted at different areas of the vagus nerve. This evidence review also addresses devices that stimulate the vagus nerve transcutaneously.

Vagus Nerve Stimulation

For individuals who have seizures refractory to medical treatment who receive vagus nerve stimulation (VNS), the evidence includes randomized controlled trials (RCTs) and multiple observational studies. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCTs have reported significant reductions in seizure frequency for patients with partial-onset seizures. The

uncontrolled studies have consistently reported large reductions in a broader range of seizure types in both adults and children. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have treatment-resistant depression who receive VNS, the evidence includes 2 RCTs evaluating the efficacy of implanted VNS for treatment-resistant depression compared to sham, 1 RCT comparing therapeutic to low-dose implanted VNS, nonrandomized comparative studies, and case series. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The sham-controlled RCTs only reported short-term results and found no significant improvement in the primary outcome. The low-dose VNS controlled trial reported no statistically significant differences between the dose groups for change in depression symptom score from baseline. Other available studies are limited by small sample sizes, potential selection and confounding biases, and lack of a control group in the case series. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have chronic heart failure who receive VNS, the evidence includes a systematic review including 4 RCTs and case series. Relevant outcomes are symptoms, change in disease status, and functional outcomes. Meta-analyses of the RCTs evaluating chronic heart failure found significant improvements in New York Heart Association functional class, quality of life, 6-minute walk-test, and N-terminal-pro brain natriuretic peptide levels in patients treated with VNS compared to control. An analysis of the ANTHEM-HF uncontrolled trial evaluated longer-term outcomes of VNS use in chronic heart failure. They found that left ventricular (LV) ejection fraction improved by 18.7%, 19.3%, and 34.4% at 12, 24, and 36 months, respectively, with high-intensity VNS. Individuals with low-intensity VNS only had significant improvement in LV ejection fraction at 24 months (12.3%). The ANTHEM-HFpEF trial found improvements in New York Heart Association functional class, quality of life, and 6-minute walk test distances in patients with preserved ejection fraction and implanted VNS. Although this data is promising, a lack of a no-VNS comparator group precludes drawing conclusions based on findings from the uncontrolled studies. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have upper-limb impairment due to stroke who receive VNS, the evidence includes 3 pilot RCTs and a systematic review of these RCTs. Relevant outcomes are symptoms, change in disease status, and functional outcomes. Two RCTs compared VNS plus rehabilitation to rehabilitation alone; 1 failed to show significant improvements for the VNS group on response and function outcomes, but the other, which had a larger patient population, found a significant difference in response and function outcomes. The other RCT compared VNS to sham and found that although VNS significantly improved response rate, there were 3 serious adverse events related to surgery. A systematic review pooling these data found that implanted VNS improved upper limb motor function based on Fugl-Meyer Assessment-Upper Extremity score when compared to control. Longer-term follow-up studies are needed to evaluate long-term efficacy and safety. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have other neurologic conditions (eg, essential tremor, headache, fibromyalgia, tinnitus, autism) who receive VNS, the evidence includes case series. Relevant outcomes are symptoms, change in disease status, and functional outcomes. Case series are insufficient to draw conclusions regarding efficacy. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Transcutaneous Vagus Nerve Stimulation

For individuals with cluster headaches who receive transcutaneous VNS (tVNS; also referred to as noninvasive VNS [nVNS]) to prevent cluster headaches, the evidence includes 1 RCT. Relevant outcomes are symptoms, change in disease status, quality of life and functional outcomes. One RCT for prevention of cluster headache showed a reduction in headache frequency but did not include a sham treatment group. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with cluster headache who receive nVNS to treat acute cluster headache, the evidence includes RCTs. Relevant outcomes are symptoms, change in disease status, quality of life and functional outcomes. The ACT1 and ACT2 RCTs compared nVNS to sham for treatment of acute cluster headache in patients including both chronic and episodic cluster headache. In ACT1, there was no statistically significant difference in the overall population in the proportion of patients with pain score of 0 or 1 at 15 minutes into the first attack and no difference in the proportion of patients who were pain-free at 15 minutes in 50% or more of the attacks. In the episodic cluster headache subgroup (n=85) both outcomes were statistically significant favoring nVNS although the interaction p-value was not reported. In ACT2, the proportion of attacks with pain intensity score of 0 or 1 at 30 minutes was higher for nVNS in the overall population (43% vs. 28%, p=.05) while the proportion of attacks that were pain-free at 15 minutes was similar in the 2 treatment groups in the overall population (14% vs. 12%). However, a statistically significantly higher proportion of attacks in the episodic subgroup (n=27) were pain-free at 15 minutes in the nVNS group compared to sham (48% vs. 6%, p<.01). These studies suggest that people with episodic and chronic cluster headaches may respond differently to acute treatment with nVNS. Studies designed to focus on episodic cluster headache are needed. Quality of life and functional outcomes have not been reported. Treatment periods ranged from only 2 weeks to 1 month with extended open-label follow-up of up to 3 months. There are few adverse events of nVNS and they are mild and transient. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with migraine headache who receive nVNS to treat acute migraine headache, the evidence includes 1 RCT. Relevant outcomes are symptoms, change in disease status, quality of life and functional outcomes. One RCT has evaluated nVNS for acute treatment of migraine with nVNS in 248 patients with episodic migraine with/without aura. There was not a statistically significant difference in the primary outcome of the proportion of participants who were pain-free without using rescue medication at 120 minutes (30% vs. 20%; p=.07). However, the nVNS group had a higher proportion of patients with decrease in pain from moderate or severe to mild or no pain at 120 minutes (41% vs. 28%; p=.03) and a higher proportion of patients who were pain-free at 120 minutes for 50% or more of their attacks (32% vs. 18%; p=.02). There are few adverse events of nVNS and they are mild and transient. Quality of life and functional outcomes were not reported and the double-blind treatment period was 4 weeks with an additional 4 weeks of open-label treatment. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with chronic migraine headache who receive nVNS to prevent migraine headache, the evidence includes 3 RCTs. Relevant outcomes are symptoms, change in disease status, quality of life and functional outcomes. The EVENT RCT was a feasibility study of prevention of migraine that was not powered to detect differences in efficacy outcomes. It does not demonstrate the efficacy of nVNS for prevention of migraine. The PREMIUM RCT was a phase 3, multicenter, sham-controlled RCT including 341 randomized participants with a 12-week double-blind treatment period. The results of PREMIUM demonstrated that nVNS was not statistically significantly superior to sham with respect to the outcomes of reduction of at least 50% in migraine days from baseline to the last 4 weeks, reduction in number of migraine days from baseline to the last 4 weeks, or acute medication days. The PREMIUM II trial was a multicenter, sham-controlled RCT including 231 randomized participants with a 12-week double-blind treatment period. The trial was terminated early due to the COVID-19 pandemic and results were based on a modified intention-to-treat population that included 113 total participants. Results demonstrated that treatment with nVNS was not statistically significantly superior to sham with respect to the primary outcome of reduction in the number of migraine days per month during weeks 9 through 12, nor other outcomes such as mean change in the number of headache days or acute medication days. However, the percentage of patients with at least a 50% reduction in the number of migraine days was significantly greater in the nVNS group than in the sham group. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have other neurologic, psychiatric, or metabolic disorders (eg, epilepsy, depression, schizophrenia, noncluster headache, impaired glucose tolerance, fibromyalgia, stroke) who receive tVNS, the evidence includes RCTs, systematic reviews of these RCTs, and case series for some of the conditions. Relevant outcomes are symptoms, change in disease status, and functional outcomes. The RCTs are all small and have various methodologic problems. None showed definitive efficacy of tVNS in

improving patient outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Policy History

Date	Action
10/2024	Clarified coding information.
4/2024	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2024	Clarified coding information.
10/2023	Clarified coding information.
4/2023	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
3/2022	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
4/2021	Annual policy review. Description, summary, and references updated. Policy statements unchanged. Clarified coding information.
1/2021	Medicare information removed. See MP #132 Medicare Advantage Management for local coverage determination and national coverage determination reference.
10/2020	Clarified coding changes.
4/2020	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
4/2019	Annual policy review. Description, summary, and references updated. Policy statements unchanged.
1/2019	Clarified coding changes.
6/2018	Annual policy review. No changes to policy statements.
5/2018	New references added from annual policy review. Background and summary clarified. Prior Authorization Information reformatted.
12/2017	Annual policy review. New investigational indications described. Clarified coding information. Effective 3/1/2018.
3/2016	Annual policy review. New references added.
5/2015	Annual policy review. New references added.
8/2014	Annual policy review. New investigational indications described. Effective 8/1/2014.
6/2014	Updated Coding section with ICD10 procedure and diagnosis codes, effective 10/2015.
12/2013	Removed the HCPCS codes (L8680-LL8689) as they do not meet the intent.
10/2013	Removed CPT codes 64569, 64570 as these CPT codes do not apply to the policy.
4/2013	Annual policy review. New references added.
2/2013	Annual policy review. Changes made to policy statements. Effective 2/4/2013.
1/2013	Updated to add new CPT codes 0312T-0317T.
11/2011-4/2012	Medical policy ICD 10 remediation: Formatting, editing and coding updates. No changes to policy statements.
4/2011	Annual policy review. No changes to policy statements.
1/2011	Reviewed - Medical Policy Group - Neurology and Neurosurgery. No changes to policy statements.
1/2010	Reviewed - Medical Policy Group - Neurology and Neurosurgery. No changes to policy statements.
1/2009	Reviewed - Medical Policy Group - Neurology and Neurosurgery. No changes to policy statements.
1/2008	Annual policy review. No changes to policy statements.
1/2008	Reviewed - Medical Policy Group - Neurology and Neurosurgery. No changes to policy statements.
7/2007	Reviewed - Medical Policy Group - Neurology and Neurosurgery. No changes to policy statements.
2/2007	Reviewed - Medical Policy Group - Psychiatry and Ophthalmology. No changes to policy statements.

Information Pertaining to All Blue Cross Blue Shield Medical Policies

Click on any of the following terms to access the relevant information:

[Medical Policy Terms of Use](#)

[Managed Care Guidelines](#)

[Indemnity/PPO Guidelines](#)

[Clinical Exception Process](#)

[Medical Technology Assessment Guidelines](#)

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