Molina Clinical Policy
Vagal Nerve Stimulation (VNS) for Epilepsy: Policy No. 006

Last Approval: 02/14/2024
Next Review Due By: February 2025

DISCLAIMER

This Molina Clinical Review (MCR) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment, and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Epilepsy is one of the most common neurological conditions worldwide characterized by recurrent seizures. Seizures are defined as paroxysmal disorders of the central nervous system characterized by abnormal cerebral neuronal discharge, with or without loss of consciousness. Most seizures can be categorized as either focal or generalized according to whether the onset of electrical activity involves both sides or a focal region of the brain. Epilepsy has a myriad of causes, such as brain tumors, metabolic disorders, hypoxic brain injuries, strokes, infections, and certain genetic syndromes; however, most cases are idiopathic in origin. Anti-epileptic medications are the first line of defense in treating the seizure disorder, however, many cases remain uncontrolled even in the setting of a rigorous drug regimen. Since epilepsy carries an increased risk for premature death, controlling the condition is paramount to patient's overall health and wellbeing.

Refractory epilepsy, also referred to as intractable or drug-resistant epilepsy, is used to characterize patients with epilepsy whose seizures do not effectively respond to anti-epileptic medications. Refractory epilepsy may affect up to 20 to 40% of epileptic patients, or about 400,000 persons in the United States, the majority of which present with partial/focal-onset seizures, especially those associated with temporal lobe epilepsy (Gummadavelli et al. 2022; Sirven 2022). Recent International League Against Epilepsy expert consensus recommendations support early referral for epilepsy resective surgery for patients with refractory epilepsy as soon as drug resistance is established, regardless of epilepsy duration, seizure type, epilepsy type, localization, or comorbidities (Jehi et al. 2022). When surgery is contraindicated or ineffective, however, vagal nerve stimulation has emerged as a treatment option.

Vagal Nerve Stimulation (VNS) is a nonpharmacologic antiepileptic therapy that involves the implantation of a subcutaneous programmable device connected to leads placed around the vagus nerve. The device is surgically implanted under local, regional, or general anesthesia and lasts 45 minutes to two hours. Most often, it is performed as an outpatient surgery, but some patients need to stay in the hospital overnight following surgery. Most reported complications associated with VNS are hoarseness, neck and throat pain, nausea, vomiting, dyspnea, and coughing. Less common complications include vocal cord paralysis, facial muscle paralysis, and infection.

Transcutaneous vagal nerve stimulation (tVNS) has been proposed as a noninvasive alternative to implantable VNS for a variety of indications such as epilepsy, major depression, 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.

Regulatory

VNS is a procedure and thus not regulated by the FDA. Any medical devices, drugs, and/or tests used as part of this procedure, on the other hand, may be subject to FDA regulation.

There are several devices FDA approved for vagal nerve stimulation under the product code LYJ (Stimulator, Autonomic Nerve, Implanted for Epilepsy) in the Premarket Approval Database on the FDA website.

tVNS devices are not currently FDA approved for the treatment of epilepsy.

COVERAGE POLICY

Implantable Vagal Nerve Stimulation for Epilepsy (VNS) **may be considered medically necessary** for patients with medically refractory partial onset seizures when **ALL** the following are met:

1. Member is 4 years or older
2. Member is being treated by a Neurologist
3. Refractory to at least one year of two or more adequately dosed antiepileptic therapy, of which the member was compliant
4. Continued seizures which have a major impact on activities of daily living
5. Ineligible for resective surgery OR has failed resective surgery
6. Procedure is conducted with an FDA-approved device
7. Diagnosis of **ONE** of the following:
    a. Focal onset or generalized onset seizures
    b. Lennox-Gastaut syndrome

Limitations and Exclusions

Transcutaneous VNS, also known as active auricular transcutaneous electrical nerve stimulation, is considered **experimental, investigational, and unproven** due to insufficient evidence in the peer reviewed scientific literature that prove safety and efficacy for any indication.

VNS Therapy is contraindicated for **ALL** the following indications:

1. Children under the age of 4 years
2. Members diagnosed with progressive metabolic or degenerative disorders that will result in continued deterioration within a 6 to 12-month time frame (e.g., malignant brain neoplasm or Rasmussen's encephalitis).
3. Members where previous bilateral or left cervical vagotomy is contraindicated.
4. Members with a cardiac pacemaker or implantable cardioverter defibrillator (ICD).
5. Requests for VNS for any condition other than medically intractable partial onset epileptic seizure disorder including, but not limited to, the following: addiction, Alzheimer's disease, anxiety, autism, bipolar disorders, bulimia, cancer, cerebral palsy, chronic heart failure, chronic refractory hiccups, coma, craving, essential tremor, fibromyalgia, headache, ischemic stroke, memory and learning disability, migraine, multiple sclerosis, narcolepsy, obesity, obsessive-compulsive disorder, panic disorder, pain syndromes, posttraumatic stress disorder, sleep disorder, traumatic brain injury, primary Sjogren's syndrome, Tourette's syndrome.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Vagal Nerve Stimulation (VNS)
Ferreira Soares and Pires de Aguiar (2023) conducted a systematic review and meta-analysis on callosotomy versus VNS in the treatment of Lennox-Gastaut syndrome. A total of 32 studies met eligibility criteria, 18 articles studied VNS with a total of 175 patients, and 14 studied corpus callosotomy with a total of 107 patients. The authors first analyzed the treatment modalities to uncover the rate at which seizures were reduced by more than or equal to 50% and found

corpus callosotomy had an incidence of 65% (95% CI, 37%-94%), with an I2 value of 82.7%; and VNS had an incidence of 34% (95% CI, 11%-57%), with an I2 value of 80.7%. Next the authors analyzed the modalities to uncover the success rate of any seizure reduction post treatment and found corpus callosotomy had an incidence of 80% (95% CI, 58%-100%), with an I2 value of 84.7%; VNS had an incidence of 64% (95% CI, 38%-89%), with an I2 value of 90.8%. The overall meta-analysis revealed both modalities to effectively reduce seizures with an overlap of confidence intervals, with no statistical difference between the treatments in both scenarios.

Mao et al. (2022) conducted a systematic review and meta-analysis comparing the short term and long-term efficacies and tolerability of vagal nerve stimulation in patients with drug resistant epilepsy. A total of 61 randomized controlled trials and observational studies were included and analyzed, totaling 5223 patients. A random-effect model was used to generate overall responder rates and overall incidences of complication. The overall responder rates at 3, 6, 12, 24, 36, 48, and 60 months postoperatively were 42%, 46%, 40%, 45%, 48%, 50% and 50% respectively. The overall reported incidence rate per complication were 27% hoarseness/voice change, 1% throat pain, 13% coughing, 1% dyspnea, 10% paresthesia, 6% muscle pain, 10% headache, 1% dysphagia, 01% neck pain, 4% infection, 3% lead fracture, 1% vocal cord palsy, and 2% device malfunction. The analysis led authors to conclude VNS is a safe and effective treatment for patients with drug resistant epilepsy.

Panebianco et al. (2022 & 2015) conducted a systematic review and meta-analysis on vagus nerve stimulation for focal seizures. The 2022 analysis focused on reviewing the literature to update the conclusions made in the 2015 analysis; however, the authors did not identify any new studies for the update, therefore the conclusions made in the 2015 analysis remain unchanged. The 2015 analysis included randomized, double-blind, parallel or crossover studies, controlled trials of VNS as add-on treatment comparing high and low stimulation paradigms (including three different stimulation paradigms - duty cycle: rapid, mid, and slow) and VNS stimulation versus no stimulation or a different intervention in patients with drug resistant partial seizures that were not eligible or had failed surgical interventions. Five 5 studies were analyzed for a total of 439 patients. The two primary outcomes assessed were: 50% or greater reduction in total seizure frequency, and adverse effects. Pooled Risk Ratios with 95% confidence intervals (95% CI) were estimated for outcomes of seizure frequency and adverse effects. The overall risk ratio (95% CI) for 50% or greater reduction in seizure frequency across all studies was 1.73 (1.13 to 2.64) showing that high frequency VNS was over one and a half times more effective than low frequency VNS. The risk ratios of adverse effects were as follows: voice alteration and hoarseness 2.17 (99% CI 1.49 to 3.17); cough 1.09 (99% CI 0.74 to 1.62); dyspnea 2.45 (99% CI 1.07 to 5.60); pain 1.01 (99% CI 0.60 to 1.68); paresthesia 0.78 (99% CI 0.39 to 1.53); nausea 0.89 (99% CI 0.42 to 1.90); headache 0.90 (99% CI 0.48 to 1.69). The authors concluded VNS for partial seizures appears to be an effective and well tolerated treatment and using the high stimulation was significantly better than low stimulation in reducing frequency of seizures. Further high-quality research is needed to validate these findings.

Klinkenberg et al. (2012) conducted a randomized controlled trial to evaluate the effects of VNS in children with intractable epilepsy on seizure frequency and severity and in terms of tolerability and safety. In this study 41 children (23 males; 18 females; mean age at implantation 11y 2mo, SD 4y 2mo, range 3y 10mo-17y 8mo) were included. Thirty-five participants had localization-related epilepsy (25 symptomatic; 10 cryptogenic), while six participants had generalized epilepsy (four symptomatic; two idiopathic). During a baseline period of 12 weeks, seizure frequency and severity were recorded using seizure diaries and the adapted Chalfont Seizure Severity Scale (NHS3), after which the participants entered a blinded active controlled phase of 20 weeks. During this phase, half of the participants received high-output VNS (maximally 1.75mA) and the other half received low-output stimulation (0.25mA). Finally, all participants received high-output stimulation for 19 weeks. For both phases, seizure frequency and severity were assessed as during the baseline period. At the end of the randomized controlled blinded phase, seizure frequency reduction of 50% or more occurred in 16% of the high-output stimulation group and in 21% of the low-output stimulation group (p=1.00). There was no significant difference in the decrease in seizure severity between participants in the stimulation groups. Overall, VNS reduced seizure frequency by 50% or more in 26% of participants at the end of the add-on phase. The overall seizure severity also improved (p<0.001). The authors concluded that VNS is a safe and well-tolerated adjunctive treatment of epilepsy in children. Our results suggest that the effect of VNS on seizure frequency in children is limited. However, the possible reduction in seizure severity and improvement in well-being makes this treatment worth considering in individual children with intractable epilepsy.

Transcutaneous Vagal Nerve Stimulation (t-VNS)
Lampros et al. (2021) conducted a systematic review on t-VNS in the treatment of epilepsy. Ten studies were included in the analysis for a total of 350 patients across all studies. The frequency of which t-VNS was applied varies across the studies from 10-30Hz, and treatment intensity was usually adjusted according to patients' preferences and pain

tolerance (around 1mA). The reviewed clinical trials produced a mean seizure frequency reduction from 30 to 65 percent. Three studies reported a statistically significant (p<0,05) improvement in patients' quality of life and two studies reported statistically significant (p<0,05) seizure severity reduction. The most common side effect was headache (8.9%), skin irritation at the placement site (7.1%) and nasopharyngitis (5.1%). No serious adverse events were reported in any study. The authors concluded that the available studies analyzed were too heterogenous to extrapolate a conclusion on t-VNS's safety and efficacy, and therefore could only offer a possible benefit to patients with refractory seizures.

National and Specialty Organizations

The **American Academy of Neurology (AAN)** evidence-based guideline on VNS for the treatment of epilepsy indicates that VNS may be considered for seizures in children, for Lennox-Gastaut syndrome (LGS) associated seizures, and for improving mood in adults with epilepsy (Level C). VNS may be considered to have improved efficacy over time (Level C). Children should be carefully monitored for site infection after VNS implantation. (Morris et al. 2013).

The **National Institute for Health and Care Excellence (NICE)** published a guideline "Epilepsies in children, young people and adults" in 2022 stating that vagal nerve stimulation in treating refractory epilepsy in children and adults is appropriate in the setting of drug resistant seizures and considers VNS an adjunctive therapy.

The **Washington State Health Authority (WSHA)** published a report in 2020 entitled *Vagal Nerve Stimulation for Epilepsy and Depression* in April 2020. The final evidence report states that "VNS appears to be an appropriate treatment option for adults and children with treatment-resistant epilepsy, but there is a lack of robust evidence on the effectiveness of VNS for TRD in adults. The use of VNS is commonly associated with minor adverse events, such as coughing and voice alteration, which are often transient and tend to decrease over time. In some cases, adverse events can be minimized through adjustment of the stimulation parameters. However, if VNS equipment or its components fail, people can be exposed to rare, but serious harms."

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology) 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
61888	Revision or removal of cranial neurostimulator pulse generator or receiver
64553	Percutaneous implantation of neurostimulator electrode array; cranial nerve
64568	Open 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/transmitter (e.g., 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 brain, cranial nerve, spinal cord, peripheral nerve, or sacral nerve, neurostimulator pulse generator/transmitter, without programming
95976	Electronic analysis of implanted neurostimulator pulse generator/transmitter (e.g., 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 (e.g., 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
0783T	Transcutaneous auricular neurostimulation, set-up, calibration, and patient education on use of equipment

HCPCS (Healthcare Common Procedure Coding System) Codes

Code	Description
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
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

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

02/14/2024	Policy reviewed. No changes to coverage criteria, updated overview, and summary of medical evidence.
02/08/2023	Policy reviewed, no changes to coverage, updated references.
02/09/2022	Policy reviewed, no changes to coverage, updated references.
02/08/2021	Policy revised to be specific to epilepsy; *MCP-393 VNS for Depression.* IRO Peer reviewed on January 7, 2021, by a practicing, board-certified physician in the areas of Neurology, Sleep Medicine.
04/23/2020	Policy reviewed, no changes to coverage, updated references.
09/18/2019	Policy reviewed, no changes to coverage, updated references.
03/08/2018	Policy reviewed, no changes to criteria. Updated references, summary of medical evidence sections.
09/19/2017	Policy reviewed, no changes to coverage, updated references.
06/15/2016	Policy reviewed, no changes to coverage, updated references.
12/16/2015	Policy reviewed, no changes to coverage, updated references.
06/12/2014	Policy reviewed, no changes to coverage, updated references.
12/14/2011	Policy reviewed and revised. Clinical criteria and coverage exclusions were updated.
06/19/2008	Policy revised.
04/25/2007	New policy.

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