Medical Policy

Responsive Neurostimulation for the Treatment of Refractory Partial Epilepsy

Table of Contents
- Policy: Commercial
- Policy: Medicare
- Authorization Information
- Coding Information
- Description
- Policy History
- Information Pertaining to All Policies
- References

Policy Number: 716
BCBSA Reference Number: 7.01.143

Related Policies
- Vagus Nerve Stimulation, #474
- Deep Brain Stimulation, #473

Policy
Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue℠ and Medicare PPO Blue℠ Members

Responsive neurostimulation may be considered MEDICALLY NECESSARY for patients with partial epilepsy who meet ALL of the following criteria:

- Are 18 years or older
- Have a diagnosis of partial-onset seizures with 1 or 2 well-localized seizure foci identified
- Have an average of 3 or more disabling seizures (eg, motor partial seizures, complex partial seizures, or secondary generalized seizures) per month over the prior 3 months
- Are refractory to medical therapy (have failed 2 or more appropriate antiepileptic medications at therapeutic doses)
- Are not candidates for focal resective epilepsy surgery (eg, have an epileptic focus near eloquent cerebral cortex; have bilateral temporal epilepsy)
- Do not have contraindications* for RNS placement.

*Contraindications for RNS placement include 3 or more specific seizure foci, presence of primary generalized epilepsy, or presence of a rapidly progressive neurologic disorder.

Responsive neurostimulation is considered INVESTIGATIONAL for all other indications.

Prior Authorization Information
Pre-service approval is required for all inpatient services for all products.
See below for situations where prior authorization may be required or may not be required.
Yes indicates that prior authorization is required.
No indicates that prior authorization is not required.
N/A indicates that this service is primarily performed in an inpatient setting.

<table>
<thead>
<tr>
<th>Commercial Managed Care (HMO and POS)</th>
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<tr>
<td>Commercial PPO and Indemnity</td>
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<td>Medicare HMO Blue℠</td>
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<td>Medicare PPO Blue℠</td>
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**CPT Codes / HCPCS Codes / ICD-9 Codes**
The following codes are included below for informational purposes. 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. A draft of future ICD-10 Coding related to this document, as it might look today, is included below for your reference.

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

**CPT Codes**
There is no specific CPT code for this procedure.

**Description**

**Overview of Seizures and Seizure Disorders**
Partial seizures arise from a discrete area of the brain and can cause a range of different symptoms, depending on the seizure type and the brain area involved. Partial seizures may be further grouped into simple partial seizures, which may be associated with motor, sensory, or autonomic symptoms, or complex partial seizures, in which patients’ consciousness is affected. Complex partial seizures may be associated with abnormal movements (automatisms). In some cases, partial seizures may result in secondary generalization, in which widespread brain electrical activity occurs after the onset of a partial seizure, thereby resulting in a generalized seizure.

Seizure disorders may be grouped into epileptic syndromes based on a number of factors, including the types of seizures that occur and their localization, the age of onset, patterns on electroencephalogram (EEG), associated clinical or neuroimaging findings, and genetic factors. Temporal lobe epilepsy is the most common syndrome associated with partial-onset seizures. Thirty percent to 40% of those with partial-onset seizures have intractable epilepsy, defined as a failure to control seizures after 2 seizure medications that have been appropriately chosen and used.1

**Epilepsy Treatment**

**Medical Therapy for Seizures**
Standard therapy for seizures, including partial seizures, includes treatment with 1 or more of variety of antiepileptic drugs (AEDs). Advances have occurred with the development and approval of newer AEDs, including oxcarbazepine, lamotrigine, topiramate, gabapentin, pregabalin, levetiracetam, tiagabine, and zonisamide.2 However, response to AEDs is less than ideal: 1 systematic review of comparisons between multiple newer AEDs for refractory partial epilepsy reported an overall average responder rate in the treatment groups of 34.8%.2 As a result, there are substantial numbers of patients who do not achieve good seizure control with medications alone.

**Surgical Therapy for Seizures**
When a discrete seizure focus can be identified, seizure control may be achieved through resection of the seizure focus (epilepsy surgery). For temporal lobe epilepsy, 1 RCT demonstrated that surgery for epilepsy was superior to prolonged medical therapy in reducing seizures associated with impaired awareness and in improving quality of life. Surgery for refractory focal epilepsy (excluding simple partial
seizures) is associated with 5-year rates of freedom from seizures of 52%, with 28% of seizure-free individuals able to discontinue AEDs. Selection of appropriate patients for epilepsy surgery is important, as those with nonlesional extratemporal lobe epilepsy have worse outcomes after surgery than those with nonlesional temporal lobe epilepsy. Some patients are not candidates for epilepsy surgery if the seizure focus is located in an eloquent area of the brain or other region that cannot be removed without risk of significant neurologic deficit.

**Neurostimulation for Neurologic Disorders**

Electrical stimulation at one of several locations has been used as therapy for epilepsy, either in addition to or as an alternative to medical or surgical therapy. Vagus nerve stimulation (VNS) has been widely used for refractory epilepsy, following FDA approval of a VNS device in 1997 and 2 RCTs evaluating VNS in epilepsy. Although the mechanism of the VNS’s therapeutic effects are not fully understood, VNS is thought to reduce seizure activity through activation of vagal visceral afferents with diffuse central nervous system projections, leading to a widespread effect on neuronal excitability.

Stimulation of other locations in the neuroaxis has been studied for a variety of neurologic disorders. Electrical stimulation at deep brain nuclei (deep brain stimulation [DBS]) involves the use of chronic, continuous stimulation of a target and has been most widely used in the treatment of Parkinson disease and other movement disorders, has also been investigated for epilepsy. DBS of the anterior thalamic nuclei has been studied in 1 RCT, the Stimulation of the Anterior Nucleus of the Thalamus for Epilepsy (SANTE) trial, but DBS is not currently approved by FDA for stimulation of the anterior thalamic nucleus. Stimulation of the cerebellar and hippocampal regions and the subthalamic, caudate, and centromedian nuclei have also been evaluated for the treatment of epilepsy.

**RNS for Epilepsy**

RNS shares some features with DBS, but is differentiated by its use of direct cortical stimulation and by the fact that the device performs both monitoring and stimulation functions. The RNS system provides stimulation in response to detection of specific epileptiform patterns, while DBS provides continuous or intermittent stimulation at preprogrammed settings.

Development of the RNS system arose out of observations related to the effects of cortical electrical stimulation for seizure localization. It has been observed that electrical cortical stimulation can terminate induced and spontaneous electrographic seizure activity in humans and animals. Patients with epilepsy may undergo implantation of subdural monitoring electrodes for the purposes of seizure localization, which at times have been used for neurostimulation to identify eloquent brain regions. Epileptiform discharges that occur during stimulation for localization can be stopped by a train of neighboring brief electrical stimulations.

In tandem with the recognition that cortical stimulation may be able to stop epileptiform discharges was the development of fast pre-ictal seizure prediction algorithms. These algorithms involve the interpretation of electrocorticographic data from detection leads over the cortex. The RNS process thus includes electrocorticographic monitoring via cortical electrodes, analysis of data through a proprietary seizure detection algorithm, and delivery of electrical stimulation via both cortical and deep implanted electrodes to attempt to halt a detected epileptiform discharge.

One system, the Neuropace RNS® System, is currently approved by FDA and is commercially available. The system consists of an implantable neurostimulator, a cortical strip lead, a depth lead, a programmer and telemetry wand, and a patient data management system. Before device implantation, the patient undergoes seizure localization, which includes inpatient video-EEG monitoring and magnetic resonance imaging for detection of epileptogenic lesions. Additional testing may also include EEG with intracranial electrodes, intraoperative or extraoperative stimulation with subdural electrodes, additional imaging studies, and/or neuropsychological testing and intracarotid amytal (Wada) testing. The selection and location of the leads are based on the location of seizure foci. Cortical strip leads are recommended for seizure foci on the cortical surface, while the depth leads are recommended for seizure foci beneath the cortical surface. The implantable neurostimulator and cortical and/or depth leads are implanted.
intracranially. The neurostimulator is initially programmed in the operating room to detect electrocorticographic activity. Responsive therapy is initially set up using standard parameters (Neuropace recommended initial settings: frequency 200 Hz; pulse width 160 μs; burst duration 100 ms; current 1.0 mA) from the electrodes from which electrical activity is detected. Over time, the responsive stimulation settings are adjusted on the basis of electrocorticography data, which are collected by the patient through interrogation of the device with the telemetry wand and transmitted to the data management system.

**Summary**

Responsive neurostimulation (RNS) for the treatment of epilepsy involves the use of 1 or more implantable electric leads that serve as both a seizure detection and neurostimulation function. The device is programmed using a proprietary algorithm to recognize seizure patterns from electrocorticography output and to deliver electrical stimulation with the goal of terminating a seizure. One device, the Neuropace RNS System, has U.S. Food and Drug Administration (FDA) approval for the treatment of refractory partial epilepsy.

The available literature related to the efficacy of RNS for partial epilepsy consists of 1 industry-sponsored randomized controlled trial (RCT), which was used for the device's FDA approval, with 2-year follow-up available. In addition, there were several case series and case reports. The available RCT is well designed and reported that RNS is associated with improvements in mean seizure frequency in patients with refractory partial epilepsy, with an absolute difference in change in seizure frequency of about 20% (approximately 5 seizures per month) between groups, but that the percent of patients who responded to treatment with at least a 50% reduction in seizures was not different from sham control. The number of adverse events (AEs) reported in the available studies is low. Although the data on AEs is limited by small numbers of patients, and follow-up beyond 2 years has not been reported, patients who are candidates for RNS are generally severely debilitated and have limited other treatment options. Results from clinical vetting indicate consensus that that the pivotal RCT demonstrated clinically meaningful results and that RNS is medically necessary for a subgroup of patients with refractory partial epilepsy. Therefore, RNS may be considered medically necessary in patients with medication-refractory partial epilepsy who are not candidates for epilepsy surgery, as outlined in the Policy statement.

**Policy History**

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<th>Date</th>
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<tr>
<td>5/2016</td>
<td>New references added from BCBSA National medical policy.</td>
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**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

**References**