



MASSACHUSETTS

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## Medical Policy

# Responsive Neurostimulation for the Treatment of Refractory Focal Epilepsy

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### Policy Number: 716

BCBSA Reference Number: 7.01.143

NCD/LCD: NA

### Related Policies

- Vagus Nerve Stimulation, [#474](#)
- Deep Brain Stimulation, [#473](#)

### Policy

#### Commercial Members: Managed Care (HMO and POS), PPO, and Indemnity Medicare HMO Blue<sup>SM</sup> and Medicare PPO Blue<sup>SM</sup> 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 focal seizures with 1 or 2 well-localized seizure foci identified;
- Have an average of 3 or more disabling seizures (eg, motor focal, complex focal, 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); and
- Do not have contraindications\* for RNS placement.

\*Contraindications for responsive neurostimulation device 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

#### 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.

	<b>Outpatient</b>
<b>Commercial Managed Care (HMO and POS)</b>	Prior authorization is <b>not required</b> .
<b>Commercial PPO and Indemnity</b>	Prior authorization is <b>not required</b> .
<b>Medicare HMO Blue<sup>SM</sup></b>	Prior authorization is <b>not required</b> .
<b>Medicare PPO Blue<sup>SM</sup></b>	Prior authorization is <b>not required</b> .

**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.*

**CPT Codes**

There is no specific CPT code for this procedure.

**Description**

**SEIZURES AND SEIZURE DISORDERS**

Focal seizures (previously referred to as partial seizures) arise from a discrete area of the brain and can cause a range of symptoms, depending on the seizure type and the brain area involved.

Note that the term *focal seizure* in older literature may be referred to as “partial seizure.” A position paper from the International League Against Epilepsy (2017) outlined updated terminology for seizure and epilepsy subtypes.<sup>1</sup> For example, focal-onset seizures are subdivided based on the associated level of consciousness, and subsequently into whether they are motor or non-motor-onset.

Focal seizures are further grouped into simple focal seizures, which may be associated with motor, sensory, or autonomic symptoms, or complex focal seizures, in which consciousness is affected. Complex focal seizures may be associated with abnormal movements (automatisms). In some cases, focal seizures may result in secondary generalization, in which widespread brain electrical activity occurs after the onset of a focal 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, associated clinical or neuroimaging findings, and genetic factors. Temporal lobe epilepsy is the most common syndrome associated with focal seizures. Of those with focal seizures, 30% to 40% have intractable epilepsy, defined as a failure to control seizures after 2 seizure medications have been appropriately chosen and used.<sup>2</sup>

**Epilepsy Treatment**

**Medical Therapy for Seizures**

Standard therapy for seizures, including focal seizures, includes treatment with one or more of various antiepileptic drugs (AEDs), which include newer AEDs, like oxcarbazepine, lamotrigine, topiramate, gabapentin, pregabalin, levetiracetam, tiagabine, and zonisamide.<sup>3</sup> Currently, response to AEDs is less than ideal: <sup>1</sup> systematic review comparing newer AEDs for refractory focal epilepsy reported an overall average responder rate in treatment groups of 34.8%.<sup>3</sup> As a result, a substantial number of patients 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, a randomized controlled trial has demonstrated that surgery for epilepsy was superior to prolonged medical therapy in reducing seizures associated with impaired awareness and in improving quality of life.<sup>4</sup> Surgery for refractory focal epilepsy (excluding simple focal seizures) is associated with 5-year freedom from seizure rates of 52%, with 28% of seizure-free individuals able to discontinue AEDs.<sup>5</sup> Selection of appropriate patients for epilepsy surgery is important, because those with nonlesional extratemporal lobe epilepsy have worse outcomes after surgery than those with nonlesional temporal lobe epilepsy.<sup>6</sup> 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 in the brain has been used as therapy for epilepsy, either as an adjunct to or as an alternative to medical or surgical therapy. Vagus nerve stimulation (VNS) has been widely used for refractory epilepsy, following Food and Drug Administration (FDA) approval of a VNS device in 1997 and 2 randomized controlled trials evaluating VNS in epilepsy.<sup>7</sup> Although the mechanism of action for VNS is 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 of deep brain nuclei (deep brain stimulation [DBS]) involves the use of chronic, continuous stimulation of a target. It has been most widely used in the treatment of Parkinson disease and other movement disorders, and has been investigated for treating epilepsy. DBS of the anterior thalamic nuclei was studied in a randomized control trial, the Stimulation of the Anterior Nucleus of the Thalamus for Epilepsy trial, but DBS is not currently approved by FDA for stimulation of the anterior thalamic nucleus.<sup>8</sup> Stimulation of the cerebellar and hippocampal regions and the subthalamic, caudate, and centromedian nuclei have also been evaluated for the treatment of epilepsy.<sup>7</sup>

### ***Responsive Neurostimulation for Epilepsy***

Responsive neurostimulation (RNS) shares some features with DBS, but is differentiated by its use of direct cortical stimulation and by its use in both monitoring and stimulation. 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 from 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.<sup>9</sup> 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.<sup>10</sup>

In tandem with the recognition that cortical stimulation can stop epileptiform discharges was development of fast pre-ictal seizure prediction algorithms. These algorithms interpret electrocorticographic data from detection leads situated 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 in an attempt to halt a detected epileptiform discharge.

One device, 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-electroencephalographic monitoring and

magnetic resonance imaging for detection of epileptogenic lesions. Additional testing may include electroencephalography with intracranial electrodes, intraoperative or extraoperative stimulation with subdural electrodes, additional imaging studies, and/or neuropsychological testing and intracarotid amygdala (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 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.<sup>11</sup>

### **RNS for Seizure Monitoring**

Although the intent of the electrocorticography component of the RNS system is to provide input as a trigger for neurostimulation, it also provides continuous seizure mapping data (chronic unlimited cortical electrocorticography) that may be used by practitioners to evaluate patients' seizures. In particular, the seizure mapping data have been used for surgical planning of patients who do not experience adequate seizure reduction with RNS placement. Several studies have described the use of RNS in evaluating seizure foci for epilepsy surgery<sup>12</sup> or for identifying whether seizure foci are unilateral.<sup>13,14</sup>

This review does not further address use of RNS exclusively for seizure monitoring.

### **Summary**

Responsive neurostimulation (RNS) for the treatment of epilepsy involves the use of one or more implantable electric leads that serve 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 approval for the treatment of refractory focal (formerly partial) epilepsy.

For individuals who have refractory focal epilepsy who receive RNS, the evidence includes an industry-sponsored randomized controlled trial, which was used for Food and Drug Administration approval of the NeuroPace RNS System, as well as case series. Relevant outcomes are symptoms, morbidity events, quality of life, and treatment-related mortality and morbidity. The pivotal trial was well-designed and well-conducted; it reported that RNS is associated with improvements in mean seizure frequency in patients with refractory focal epilepsy, with an absolute difference in change in seizure frequency of about 20% between groups, though the percentage of treatment responders with at least a 50% reduction in seizures did not differ from sham control. Overall, the results suggested a modest reduction in seizure frequency in a subset of patients. The number of adverse events reported in the available studies is low, although the data on adverse events were limited because small study samples. Generally, patients who are candidates for RNS are severely debilitated and have few other treatment options, so the benefits are likely high relative to the risks. In particular, patients who are not candidates for resective epilepsy surgery and have few treatment options may benefit from RNS. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Consensus input from clinical vetting recommended that RNS is medically necessary for a subgroup of patients with refractory focal epilepsy. Therefore, RNS may be considered medically necessary in patients with medication-refractory focal epilepsy who are not candidates for epilepsy surgery.

### **Policy History**

<b>Date</b>	<b>Action</b>
6/2018	BCBSA National medical policy review. Policy clarified: partial epilepsy changed to focal epilepsy throughout text and title to be consistent with current terminology. Prior Authorization Information reformatted.

5/2017	New references added from BCBSA National medical policy.
5/2016	New references added from BCBSA National medical policy.
4/2015	New medical policy describing medically necessary and investigational indications. Effective 4/1/2015.

## 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

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