

**MEDICAL POLICY**

<b>POLICY TITLE</b>	<b>RESPONSIVE NEUROSTIMULATION FOR THE TREATMENT OF REFRACTORY FOCAL EPILEPSY</b>
<b>POLICY NUMBER</b>	<b>MP 1.156</b>

<b>CLINICAL BENEFIT</b>	<input checked="" type="checkbox"/> MINIMIZE SAFETY RISK OR CONCERN. <input type="checkbox"/> MINIMIZE HARMFUL OR INEFFECTIVE INTERVENTIONS. <input type="checkbox"/> ASSURE APPROPRIATE LEVEL OF CARE. <input type="checkbox"/> ASSURE APPROPRIATE DURATION OF SERVICE FOR INTERVENTIONS. <input checked="" type="checkbox"/> ASSURE THAT RECOMMENDED MEDICAL PREREQUISITES HAVE BEEN MET. <input type="checkbox"/> ASSURE APPROPRIATE SITE OF TREATMENT OR SERVICE.
<b>Effective Date:</b>	<b>4/1/2024</b>

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**I. POLICY**

Responsive neurostimulation may be considered **medically necessary** for patients with focal epilepsy who meet **all** of the following criteria:

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

Responsive neurostimulation is considered **investigational** for all other indications. All other indications of responsive neurostimulation other than those described in the policy section are considered investigational, as there is insufficient evidence to support a general conclusion concerning the health outcomes or benefits associated with this procedure.

**II. POLICY GUIDELINES**

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.

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***Cross-reference:***

**MP 1.042** Deep Brain Stimulation

### III. PRODUCT VARIATIONS

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This policy is only applicable to certain programs and products administered by Capital Blue Cross and subject to benefit variations as discussed in Section VI. Please see additional information below.

**FEP PPO:**

Refer to FEP Medical Policy Manual. The FEP Medical Policy manual can be found at:

<https://www.fepblue.org/benefit-plans/medical-policies-and-utilization-management-guidelines/medical-policies>.

### IV. DESCRIPTION/BACKGROUND

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**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. 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.

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.

**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. Currently, response to AEDs is less than ideal: 1 systematic review comparing newer AEDs for refractory focal epilepsy reported an overall average responder rate in treatment groups of 34.8%. As a

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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. 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. 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. 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. 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. Stimulation of the cerebellar and hippocampal regions and the subthalamic, caudate, and centromedian nuclei have also been evaluated for the treatment of epilepsy.

**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.

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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. 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 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.

**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 or for identifying whether seizure foci are unilateral.

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

**Regulatory Status**

In November 2013, the NeuroPace RNS® System (NeuroPace) was approved by FDA through the premarket approval process for the following indication.

“The RNS® System is an adjunctive therapy in reducing the frequency of seizures in individuals 18 years of age or older with partial onset seizures who have undergone diagnostic testing that localized no more than 2 epileptogenic foci, are refractory to two or more antiepileptic medications, and currently have frequent and disabling seizures (motor partial seizures, complex partial seizures and/ or secondarily generalized seizures). The RNS® System has demonstrated safety and effectiveness in patients who average 3 or more disabling seizures per month over the three most recent months (with no month with fewer than two seizures), and has not been evaluated in patients with less frequent seizures.”

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FDA product code: PFN.

**V. RATIONALE**

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**Summary of Evidence**

For individuals who have refractory focal epilepsy who receive RNS, the evidence includes an industry-sponsored RCT, which was used for Food and Drug Administration approval of the NeuroPace RNS System, as well as several published follow-up analyses. Relevant outcomes are symptoms, morbid events, quality of life, and treatment-related mortality and morbidity. The randomized controlled 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; however, 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.

**VI. DEFINITIONS**

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NA

**VII. BENEFIT VARIATIONS**

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The existence of this medical policy does not mean that this service is a covered benefit under the member's health benefit plan. Benefit determinations should be based in all cases on the applicable health benefit plan language. Medical policies do not constitute a description of benefits. A member's health benefit plan governs which services are covered, which are excluded, which are subject to benefit limits and which require preauthorization. There are different benefit plan designs in each product administered by Capital Blue Cross. Members and providers should consult the member's health benefit plan for information or contact Capital Blue Cross for benefit information.

**VIII. DISCLAIMER**

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*This is a new treatment. This policy may be subject to change due to additional data, information and feedback received. Please check for updates.*

*Capital Blue Cross's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical*

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*policy and a member's benefit information, the benefit information will govern. If a provider or a member has a question concerning the application of this medical policy to a specific member's plan of benefits, please contact Capital Blue Cross' Provider Services or Member Services. Capital Blue Cross considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.*

### IX. CODING INFORMATION

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**Note:** This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

#### Covered when medically necessary:

Procedure Codes							
L8680	L8686	L8688	61850	61860	61863	61864	61880
61885	61886	61888	61889	61891	61892	95970	95971

ICD-10-CM Diagnosis Code	Description
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



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<b>ICD-10-CM Diagnosis Code</b>	<b>Description</b>
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.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

**X. REFERENCES**

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### XI. POLICY HISTORY

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<b>MP 1.156</b>	<b>4/10/2020 Major review.</b> New policy adopted from BCBSA to provide coverage criteria for neurostimulation in patients with epilepsy refractory to other treatment.
	<b>5/21/2021 Consensus review.</b> BCBSA full adoption. No change to policy statement. Coding and References reviewed.
	<b>6/17/2021 Consensus review.</b> No changes to policy statement. FEP and references updated. Coding reviewed.
	<b>8/23/2023- Admin Review.</b> New ICD 10 codes added to the policy.
	<b>12/12/2023 Admin Review.</b> Added codes 61889, 61891, and 61892 as MN, effective 1/1/2024.
	<b>1/10/2024 Consensus Review.</b> Updated rationale, references. Coding reviewed, no changes.

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