

Responsive Neurostimulation for the Treatment of Refractory Focal Epilepsy

Policy # 00674

Original Effective Date: 11/01/2019

Current Effective Date: 08/01/2026

Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

Investigational or experimental services are not covered. This includes any drug, device, procedure, or service provided under the investigational arm of a clinical trial or clinical study. These services are excluded from coverage under benefits.

Note: Vagus Nerve Stimulation is addressed separately in medical policy 00134.

Note: Deep Brain Stimulation is addressed separately in medical policy 00024

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Company may consider responsive neurostimulation for individuals with focal epilepsy to be **eligible for coverage**** when **ALL** of the following criteria are met:

- 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 (eg, 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 greater than or equal to 2 appropriate antiepileptic medications at therapeutic doses); **AND**
- Are not candidates for focal resective epilepsy surgery (eg, have an epileptic focus near the eloquent cerebral cortex; have bilateral temporal epilepsy); **AND**
- Do not have contraindications for responsive neurostimulation device placement including **ANY** of the following:
 - o Having 3 or more specific seizure foci; **OR**
 - o Presence of primary generalized epilepsy; **OR**
 - o Presence of a rapidly progressive neurologic disorder.

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When Services Are Considered Not Medically Necessary

The use of responsive neurostimulation when patient selection criteria are not met is considered to be **not medically necessary**.**

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers responsive neurostimulation for all other indications to be **investigational**.*

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.

Background/Overview

Epilepsy Treatment

Medical Therapy for Focal Seizures

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.

Standard therapy for seizures, including focal seizures, includes treatment with 1 or more of various antiepileptic drugs, which include newer antiepileptic drugs, such as oxcarbazepine, lamotrigine, topiramate, gabapentin, pregabalin, levetiracetam, tiagabine, and zonisamide. Currently, response to antiepileptic drugs is less than ideal: 1 systematic review comparing newer antiepileptic drugs for refractory focal epilepsy reported an overall average responder rate in treatment groups of 34.8%. As a result, a substantial number of individuals 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 antiepileptic drugs. Selection of appropriate individuals for epilepsy surgery is important, because those with non-lesional extratemporal lobe epilepsy have worse outcomes after surgery than those with non-lesional temporal lobe epilepsy. Some individuals 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.

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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 has been widely used for refractory epilepsy, following U.S. Food and Drug Administration (FDA) approval of a vagus nerve stimulation device in 1997 and 2 randomized controlled trials evaluating vagus nerve stimulation in epilepsy. Although the mechanism of action for vagus nerve stimulation is not fully understood, vagus nerve stimulation 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 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 responsive neurostimulation system provides stimulation in response to detection of specific epileptiform patterns, while DBS provides continuous or intermittent stimulation at preprogrammed settings.

Development of the responsive neurostimulation 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. Individuals 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 the development of fast pre-ictal seizure prediction algorithms. These algorithms interpret electrocorticographic data from detection leads situated over the cortex. The responsive neurostimulation 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.

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Responsive Neurostimulation for Seizure Monitoring

Although the intent of the electrocorticography component of the responsive neurostimulation 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 individuals' seizures. In particular, the seizure mapping data have been used for surgical planning of individuals who do not experience adequate seizure reduction with responsive neurostimulation placement. Several studies have described the use of responsive neurostimulation in evaluating seizure foci for epilepsy surgery or for identifying whether seizure foci are unilateral.

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

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

In November 2013, the NeuroPace RNS System (NeuroPace) was approved by the 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 2 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 3 most recent months (with no month with fewer than 2 seizures) and has not been evaluated in patients with less frequent seizures.”

FDA product code: PFN.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

Approximately one-third of individuals with epilepsy do not respond to typical first-line therapy with antiepileptic medications. Seizures that occur in these individuals are referred to as refractory or drug-resistant. In individuals with refractory epilepsy, combination antiepileptic therapy often results in increased risk of adverse events. Other nonpharmacologic treatment options are available, including surgical approaches, ketogenic diet, and responsive neurostimulation. One responsive neurostimulation device, the NeuroPace RNS System, has U.S. Food and Drug Administration (FDA) approval for the treatment of refractory focal (formerly partial) epilepsy.

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Summary of Evidence

For individuals who have refractory focal epilepsy who receive responsive neurostimulation, the evidence includes an industry-sponsored randomized controlled trial (RCT), which was used for Food and Drug Administration (FDA) approval of the NeuroPace RNS System, as well as several published follow-up analyses, and several systematic reviews and meta-analyses. Relevant outcomes are symptoms, morbid events, quality of life, and treatment-related mortality and morbidity. The RCT was well-designed and well-conducted; it reported that responsive neurostimulation is associated with improvements in mean seizure frequency in individuals 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 individuals. With respect to safety, rates of serious adverse events were relatively low in the short-term pivotal trial; however, long-term follow-up to 9 years identified a cumulative serious device-related implantation site infection rate of 12.1%, and elective explantation of the neurostimulator, leads, or both was also reported as a serious device-related adverse event in at least 5% of individuals. No serious adverse events related to stimulation were reported over the 9-year follow-up period. Generally, individuals who are candidates for responsive neurostimulation are severely debilitated and have few other treatment options, so the benefits are likely high relative to the risks. In particular, individuals who are not candidates for resective epilepsy surgery and have few treatment options may benefit from responsive neurostimulation. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Supplemental Information

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in ‘Supplemental Information’ if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

No relevant clinical practice guidelines were identified.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

Ongoing and Unpublished Clinical Trials

Ongoing and unpublished trials that might influence this review are shown in Table 1.

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Table 1. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
<i>Ongoing</i>			
NCT02403843 ^a	RNS System Post-Approval Study in Epilepsy	375	Jan 2026
<i>Unpublished</i>			
NCT04839601 ^a	RNS System RESPONSE Study	9 (actual)	May 2025 (terminated; inadequate enrollment)

NCT: national clinical trial.

^a Denotes industry-sponsored or cosponsored trial.

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08/01/2019	Medical Policy Committee review
08/14/2019	Medical Policy Implementation Committee approval. New policy.
08/06/2020	Medical Policy Committee review
08/12/2020	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/05/2021	Medical Policy Committee review
08/11/2021	Medical Policy Implementation Committee approval. Coverage eligibility unchanged. Title changed to track BCBSA.
07/07/2022	Medical Policy Committee review
07/13/2022	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
07/06/2023	Medical Policy Committee review
07/12/2023	Medical Policy Implementation Committee approval. Title changed to Responsive Neurostimulation for the Treatment of Refractory Focal Epilepsy.
07/02/2024	Medical Policy Committee review
07/10/2024	Medical Policy Implementation Committee approval. No change to coverage.
07/03/2025	Medical Policy Committee review
07/09/2025	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
07/02/2026	Medical Policy Committee review
07/08/2026	Medical Policy Implementation Committee review
07/16/2026	Medical Quality Management Committee approval. The following statement was changed from investigational to not medically necessary: "The use of responsive neurostimulation when patient selection criteria are not met is considered to be not medically necessary."

Next Scheduled Review Date: 07/2027

Coding

The five character codes included in the Louisiana Blue Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)†, copyright 2025 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

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contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	61850, 61860, 61863, 61864, 61880, 61885, 61886, 61888, 61889, 61891, 61892, 95836, 95970, 95971
HCPCS	L8680, L8686, L8688
ICD-10 Diagnosis	All Related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
 1. Consultation with technology evaluation center(s);
 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
 3. Reference to federal regulations.

**Medically Necessary (or “Medical Necessity”) - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

- A. In accordance with nationally accepted standards of medical practice;
- B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
- C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

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For these purposes, “nationally accepted standards of medical practice” means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient’s health insurance contract contains language that differs from the BCBSLA Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

NOTICE: If an authorization for an ongoing course of treatment has been provided to a member and the member changes from one health plan to another health plan (e.g., a member moves from carrier A to Louisiana Blue), Louisiana Blue may honor the previous health plan’s authorization for the same service under the same type of in-network benefit for a 90-day transition period. Documentation of the authorization for the ongoing course of treatment from the previous health plan must be provided to us by the member or their provider and the services provided for the course of treatment must otherwise be a covered service under the Louisiana Blue health plan. This provision does not apply to medications covered under the plan’s pharmacy benefit.