Responsive neurostimulation (RNS) is a treatment that is used for focal epilepsy. (Focal epilepsy used to be called partial epilepsy.) The goal of RNS is to disrupt unusual electrical signals in the brain that trigger seizures. A stimulator is implanted and one or two wires are placed at the location in the brain where seizures start. When the unit detects patterns that could lead to a seizure, it sends electrical signals to interrupt a seizure before it begins. RNS may be an option when medications aren’t able to control symptoms. This policy describes when RNS may be considered medically necessary.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Medical Necessity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responsive neurostimulation (RNS)</td>
<td>Responsive neurostimulation (RNS) may be considered medically necessary for patients with focal epilepsy who meet ALL of the following criteria:</td>
</tr>
<tr>
<td></td>
<td>• Are 18 years or older</td>
</tr>
<tr>
<td></td>
<td>• Have a diagnosis of focal seizures with one or two well-localized seizure foci identified</td>
</tr>
<tr>
<td></td>
<td>• Have had an average of three or more disabling seizures (eg, motor focal seizures, complex focal seizures, or secondary generalized seizures) per month over the prior three months</td>
</tr>
<tr>
<td></td>
<td>• Are refractory to medical therapy (have failed &gt;2 appropriate antiepileptic medications at therapeutic doses)</td>
</tr>
<tr>
<td></td>
<td>• Are not candidates for focal resective epilepsy surgery (eg, have an epileptic focus near the eloquent cerebral cortex; have bilateral temporal epilepsy)</td>
</tr>
<tr>
<td></td>
<td>• Do not have contraindications for RNS device placement:</td>
</tr>
<tr>
<td></td>
<td>o Three or more specific seizure foci</td>
</tr>
<tr>
<td></td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td>o Presence of primary generalized epilepsy</td>
</tr>
<tr>
<td></td>
<td>OR</td>
</tr>
<tr>
<td></td>
<td>o Presence of a rapidly progressive neurologic disorder</td>
</tr>
<tr>
<td></td>
<td>Responsive neurostimulation (RNS) is considered investigational for all other indications.</td>
</tr>
</tbody>
</table>

Documentation Requirements

The patient’s medical records submitted for review for all conditions should document that medical necessity criteria are met. The record should include clinical documentation of:

- Diagnosis/condition
- History and physical examination documenting the severity of the condition
- Prior medical therapy that has failed
- Contraindications to focal resective epilepsy surgery

Coding
<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>61850</td>
<td>Twist drill or burr hole(s) for implantation of neurostimulator electrodes, cortical</td>
</tr>
<tr>
<td>61860</td>
<td>Craniectomy or craniotomy for implantation of neurostimulator electrodes, cerebral, cortical</td>
</tr>
<tr>
<td>61863</td>
<td>Twist drill, burr hole, craniotomy, or craniectomy with stereotactic implantation of neurostimulator electrode array in subcortical site (eg, thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), without use of intraoperative microelectrode recording; first array</td>
</tr>
<tr>
<td>61864</td>
<td>Twist drill, burr hole, craniotomy, or craniectomy with stereotactic implantation of neurostimulator electrode array in subcortical site (eg, thalamus, globus pallidus, subthalamic nucleus, periventricular, periaqueductal gray), without use of intraoperative microelectrode recording; each additional array (List separately in addition to primary procedure)</td>
</tr>
<tr>
<td>61885</td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to a single electrode array</td>
</tr>
<tr>
<td>61886</td>
<td>Insertion or replacement of cranial neurostimulator pulse generator or receiver, direct or inductive coupling; with connection to 2 or more electrode arrays</td>
</tr>
</tbody>
</table>

**HCPCS**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1767</td>
<td>Generator, neurostimulator (implantable), nonrechargeable</td>
</tr>
<tr>
<td>C1778</td>
<td>Lead, neurostimulator (implantable)</td>
</tr>
<tr>
<td>L8680</td>
<td>Implantable neurostimulator electrode, each</td>
</tr>
<tr>
<td>L8686</td>
<td>Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension</td>
</tr>
<tr>
<td>L8688</td>
<td>Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension</td>
</tr>
</tbody>
</table>

**Note:** CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

**Related Information**

N/A
Description

Approximately one-third of patients with epilepsy do not respond to typical first-line therapy with antiepileptic medications. Seizures that occur in these patients are referred to as refractory or drug-resistant. In patients 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.

Background

Epilepsy Treatment

Medical Therapy for Seizures

Standard therapy for seizures, including focal seizures, includes treatment with one or more various antiepileptic drugs (AEDs), which include newer AEDs, such as oxcarbazepine, lamotrigine, topiramate, gabapentin, pregabalin, levetiracetam, tiagabine, and zonisamide.1 Currently, response to AEDs is less than ideal: one systematic review comparing newer AEDs for refractory focal epilepsy reported an overall average responder rate in treatment groups of 34.8%.1 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 demonstrated that surgery for epilepsy was superior to prolonged medical therapy in reducing seizures associated with impaired awareness and in improving quality of life.2 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.3 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.\textsuperscript{4} 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 FDA approval of a VNS device in 1997 and two randomized controlled trials evaluating VNS in epilepsy.\textsuperscript{5} Although the mechanism of the 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 at 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 epilepsy. DBS of the anterior thalamic nuclei has been 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.\textsuperscript{6} Stimulation of the cerebellar and hippocampal regions and the subthalamic, caudate, and centromedian nuclei have also been evaluated for the treatment of epilepsy.\textsuperscript{5}

**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.\textsuperscript{7} 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.\(^8\)

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 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\(^\circledR\) System, is currently approved by FDA and is commercially available.

**Responsive Neurostimulation 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 the RNS in evaluating seizure foci for epilepsy surgery\(^9\) or for identifying whether seizure foci are unilateral.\(^10,11\)

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

**Summary of Evidence**

For individuals with refractory focal epilepsy who receive RNS, the evidence includes an industry-sponsored randomized controlled trial (RCT), which was used for FDA approval of the NeuroPace RNS\(^\circledR\) System, as well as case series. 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 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 of 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 an improvement in the net health outcome.

### Ongoing and Unpublished Clinical Trials

Some currently ongoing trials that might influence this review are listed in **Table 1**.

<table>
<thead>
<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>NCT02403843</td>
<td>RNS® System Post-Approval Study in Epilepsy</td>
<td>375</td>
<td>May 2023</td>
</tr>
</tbody>
</table>

NCT: national clinical trial

*a Denotes industry-sponsored or cosponsored trial

### Clinical Input from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

Clinical input was sought to help determine whether the use of RNS for individuals with refractory focal epilepsy would provide a clinically meaningful improvement in net health outcome and whether the use is consistent with generally accepted medical practice. In response to requests, clinical input was received from 7 respondents, including 3 specialty society-level responses from 2 specialty medical societies and 4 physician-level responses identified through 5 academic medical centers.
For individuals who have refractory focal epilepsy who receive RNS, clinical input supports this use provides a clinically meaningful improvement in net health outcome and indicates this use is consistent with generally accepted medical practice in a subgroup of appropriately selected patients. The following patient selection criteria are based on clinical expert opinion and information from clinical study populations: patients with focal epilepsy with 1 to 2 foci who are not candidates for resective epilepsy surgery.

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Guidelines or position statements will be considered for inclusion if they were issued by, or jointly by, a U.S. professional society, an international society with U.S. 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.

American Academy of Neurology

In 2013, guidelines on vagus nerve stimulation (VNS) for the treatment of epilepsy were issued by the American Academy of Neurology, which were reaffirmed in 2019.27 The guidelines made the following recommendations:

VNS may be considered for seizures in children, for LGS [Lennox-Gastaut syndrome]-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.

The Academy indicated that more information would be needed on the treatment of primary generalized epilepsy in adults (only one class II article addressed this population). The RNS system was not mentioned in these guidelines.
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.

Regulatory Status

In November 2013, the NeuroPace RNS® System (NeuroPace) was approved by the FDA through the premarket approval process for the following indication12.

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 two 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 three 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.

FDA product code: PFN.

References


<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>01/13/15</td>
<td>New Policy. Policy created with literature review through June 30, 2014 and review of clinical input. Responsive neurostimulation may be considered medically necessary for refractory partial epilepsy when criteria are met. Reformatted the policy guidelines for improved clarification.</td>
</tr>
<tr>
<td>07/01/16</td>
<td>Annual Review, approved on June 14, 2016. Policy updated with literature review through February 9, 2016; references 12 and 16-20 added. Policy statements unchanged.</td>
</tr>
<tr>
<td>07/01/18</td>
<td>Annual Review, approved June 22, 2018. Policy updated with literature review through February 2018; no references added. Policy statements unchanged. Term “partial epilepsy” changed to “focal epilepsy” throughout text and title to be consistent with current terminology. Removed CPT codes 95970 and 95971.</td>
</tr>
<tr>
<td>04/01/19</td>
<td>Minor update, added Documentation Requirements section.</td>
</tr>
<tr>
<td>07/01/19</td>
<td>Annual Review, approved June 4, 2019. Policy updated with literature review through February 2019; no references added. Policy statements unchanged.</td>
</tr>
<tr>
<td>04/01/20</td>
<td>Delete policy, approved March 10, 2020. This policy will be deleted effective July 2, 2020, and replaced with InterQual criteria for dates of service on or after July 2, 2020.</td>
</tr>
<tr>
<td>07/02/20</td>
<td>Delete policy.</td>
</tr>
<tr>
<td>07/01/21</td>
<td>Annual Review, approved June 1, 2021. Policy updated with literature review through March 8, 2021; references added. Policy statements unchanged. Added HCPC codes C1767 and C1778.</td>
</tr>
</tbody>
</table>

**Disclaimer:** This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. The Company adopts policies after careful review of published peer-reviewed scientific literature, national guidelines and local standards of practice. Since medical technology is constantly changing, the Company reserves the right to review and update policies as appropriate. Member contracts differ in their benefits. Always consult the member benefit booklet or contact a member service representative to determine coverage for a specific medical service or supply.
Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.
Discrimination is Against the Law

Premera Blue Cross complies with applicable Federal civil rights laws and does not discriminate on the basis of race, color, national origin, age, disability, or sex. Premera does not exclude people or treat them differently because of race, color, national origin, age, disability or sex.

Premera:
• Provides free aids and services to people with disabilities to communicate effectively with us, such as:
  • Qualified sign language interpreters
  • Written information in other formats (large print, audio, accessible
    electronic formats, other formats)
• Provides free language services to people whose primary language is not
  English, such as:
  • Qualified interpreters
  • Information written in other languages

If you need these services, contact the Civil Rights Coordinator.

If you believe that Premera has failed to provide these services or

discriminated in another way on the basis of race, color, national origin, age,

disability, or sex, you can file a grievance with:

Civil Rights Coordinator - Complaints and Appeals
PO Box 91102, Seattle, WA 98111
Toll free 855-332-4535, Fax 425-918-5592, TTY 800-842-5357
Email AppealsDepartmentInquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filling a grievance, the Civil Rights Coordinator is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at

https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue SW, Room 509F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at


Getting Help in Other Languages

This Notice has Important Information. This notice may have important information about your application or coverage through Premera Blue Cross. There may be key dates in this notice. You may need to take action by certain deadlines to keep your health coverage or help with costs. You have the right to get this information and help in your language at no cost.

Call 800-722-1471 (TTY: 800-842-5357).

Arabic (Arabic):

هي قلبي هذا الإشعار المعلوماتية. قد يحتوي هذا الإشعار المعلوماتية مهمة عن صحة طبية أو

العملية التي تريد الحصول عليها من خلال

Premera Blue Cross. قد تكون هناك تأثيرات محددة

لم تحملت هذه المعلومات. تأكد من فهمك هذه المعلومات ومساعدتك

لم تخلص إلى فهمك هذه المعلومات. تأكد من فهمك هذه المعلومات. اتصل

800-722-1471 (TTY: 800-842-5357).

中文 (Chinese):

本通知有重要的讯息。本通知可能有關於您透過 Premera Blue Cross 提交的申請或保險的重要訊息。本通知內可能有重要日期。您可能需要在截止日期之前採取行動。以保留您的健康保險或費用補貼。您有權利免費以您的母語得到本訊息和幫助。請撥電話 800-722-1471 (TTY: 800-842-5357).

Oromo (Cushite):


French (Français):


Deutsche (German):


Kreyòl ayisyen (Creole):


Italiano (Italian):

Este aviso contiene información importante. Es posible que este aviso contenga información importante acerca de su solicitud o cobertura a través de Premera Blue Cross. Es posible que haya fechas clave en este aviso. Es posible que deba tomar alguna medida antes de determinadas fechas para mantener su cobertura médica o ayuda con los costos. Usted tiene derecho a recibir esta información y ayuda en su idioma sin costo alguno. Llame al 800-722-1471 (TTY: 800-842-5357).

태갈로그어 (Tagalog): Ang Paunawa na ito ay naglalaman ng mahalagang impormasyon. Ang paunawa na ito ay naglalaman ng mahalagang impormasyon tungkol sa iyong aplikasyon o pagsakop sa prestandard ng Premera Blue Cross. Ang pagmamalari ng gabay at secure ang iyong pagsakop sa kahalagahan o tulong na hula ng kalooban o hanggan ng kalooban ng iyong pagsagot. Kaso ang paunawa na ito ay maaaring naglalaman ng mahalagang impormasyon.

ไทย (Thai): ประกาศนี้มีข้อมูลที่สำคัญเกี่ยวกับการขอรับการช่วยเหลือหรือการประกันสุขภาพของคุณผ่าน Premera Blue Cross และการมีความต้องการในการชำระเงินค่าบริการ คุณควรเข้าใจความเสี่ยงในการกำหนดระยะเวลาที่แน่นอนเพื่อจะสามารถขอรับการประกันสุขภาพของคุณตามสัญญาที่มีอยู่ได้ คุณไม่ต้องจ่ายค่าบริการสุขภาพและข้อมูลที่เกี่ยวข้องในการขอรับการช่วยเหลือได้ โทรต่อ 800-722-1471 (TTY: 800-842-5357)