MEDICAL POLICY – 2.02.33
Phrenic Nerve Stimulation for Central Sleep Apnea

BCBSA Ref. Policy: 2.02.33
Effective Date: Nov. 1, 2019
Last Revised: July 9, 2019
Replaces: N/A

RELATED MEDICAL POLICIES:
None

Select a hyperlink below to be directed to that section.

POLICY CRITERIA | CODING | RELATED INFORMATION
EVIDENCE REVIEW | REFERENCES | HISTORY

Clicking this icon returns you to the hyperlinks menu above.

Introduction

Central sleep apnea is a sleep disorder in which the brain briefly stops sending signals to the muscles that govern breathing. The typical way of treating central sleep apnea is to use a positive airway pressure device to blow pressurized air into the airway during sleep. A new technique of trying to treat sleep apnea is being studied. This technique calls for a specific nerve in the chest, the phrenic nerve, to be stimulated. A device is implanted and low levels of electricity are sent to the phrenic nerve. This is then supposed to stimulate the diaphragm. (The diaphragm is a large muscle beneath the lungs that expands and contracts as you breathe.) It’s thought that stimulating the diaphragm improves breathing during sleep. Phrenic nerve stimulation for central sleep apnea is investigational (unproven). More research is needed to see if this technique is safe, reliable, and effective.

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.
Service | Investigational
--- | ---
Phrenic nerve stimulation | The use of phrenic nerve stimulation for central sleep apnea is considered investigational in all situations.

### Coding

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT</td>
<td></td>
</tr>
<tr>
<td>0424T</td>
<td>Insertion or replacement of neurostimulator system for treatment of central sleep apnea; complete system (transvenous placement of right or left stimulation lead, sensing lead, implantable pulse generator)</td>
</tr>
<tr>
<td>0425T</td>
<td>Insertion or replacement of neurostimulator system for treatment of central sleep apnea; sensing lead only</td>
</tr>
<tr>
<td>0426T</td>
<td>Insertion or replacement of neurostimulator system for treatment of central sleep apnea; stimulation lead only</td>
</tr>
<tr>
<td>0427T</td>
<td>Insertion or replacement of neurostimulator system for treatment of central sleep apnea; pulse generator only</td>
</tr>
<tr>
<td>0428T</td>
<td>Removal of neurostimulator system for treatment of central sleep apnea; pulse generator only</td>
</tr>
<tr>
<td>0429T</td>
<td>Removal of neurostimulator system for treatment of central sleep apnea; sensing lead only</td>
</tr>
<tr>
<td>0430T</td>
<td>Removal of neurostimulator system for treatment of central sleep apnea; stimulation lead only</td>
</tr>
<tr>
<td>0431T</td>
<td>Removal and replacement of neurostimulator system for treatment of central sleep apnea, pulse generator only</td>
</tr>
<tr>
<td>0432T</td>
<td>Repositioning of neurostimulator system for treatment of central sleep apnea; stimulation lead only</td>
</tr>
<tr>
<td>0433T</td>
<td>Repositioning of neurostimulator system for treatment of central sleep apnea; sensing lead only</td>
</tr>
<tr>
<td>0434T</td>
<td>Interrogation device evaluation implanted neurostimulator pulse generator system for central sleep apnea</td>
</tr>
<tr>
<td>0435T</td>
<td>Programming device evaluation of implanted neurostimulator pulse generator system for central sleep apnea; single session</td>
</tr>
<tr>
<td>0436T</td>
<td>Programming device evaluation of implanted neurostimulator pulse generator system for central sleep apnea; during sleep study</td>
</tr>
</tbody>
</table>
Description

Central sleep apnea (CSA) is characterized by sleep-disordered breathing due to diminished or absent respiratory effort. CSA may be idiopathic or secondary (associated with Cheyne-Stokes breathing, a medical condition, drugs, or high altitude breathing). The use of positive airway pressure devices is currently the most common form of therapy for CSA. An implantable device that stimulates the phrenic nerve in the chest is a potential alternative treatment. The battery-powered device sends signals to the diaphragm in order to stimulate breathing and normalize sleep-related breathing patterns.

Background

Central Sleep Apnea

CSA is characterized by repetitive cessation or decrease in both airflow and ventilatory effort during sleep. CSA may be idiopathic or secondary (associated with Cheyne-Stokes breathing, a medical condition, drugs, or high altitude breathing. Cheyne-Stokes breathing is common among patients with heart failure (HF) or who have had strokes and accounts for about half of the population with CSA. CSA is less common than obstructive sleep apnea. Based on analyses of a large community-based cohort in the Sleep Heart Health Study, the estimated prevalence of CSA and obstructive sleep apnea are 0.9% and 47.6%, respectively.¹ Risk factors for CSA include age (>65 years), male gender, history of heart failure (HF), history of stroke, other medical conditions (acromegaly, renal failure, atrial fibrillation, low cervical tetraplegia, and primary mitochondrial diseases), and opioid use. Individuals with CSA have difficulty maintaining sleep
and therefore experience excessive daytime sleepiness, poor concentration, morning headaches, and are at higher risk for accidents and injuries.

**Treatment**

The goal of treatment is to normalize sleep-related breathing patterns. Because most cases of CSA are secondary to an underlying condition, central nervous system pathology, or medication side effects, treatment of the underlying condition or removal of the medication, may improve CSA.

Treatment recommendations differ depending on the classification of CSA as either hyperventilation-related (most common, including primary CSA and those relating to HF or high altitude breathing) or hypoventilation-related (less common, relating to central nervous system diseases or use of nervous system suppressing drugs such as opioids).

For patients with hyperventilation-related CSA, continuous positive airway pressure (CPAP) is considered first-line therapy. Due to CPAP discomfort, patient compliance may become an issue. Supplemental oxygen during sleep may be considered for patients experiencing hypoxia during sleep or who cannot tolerate CPAP. Patients with CSA due to HF and with an ejection fraction >45% and who are not responding with CPAP and oxygen therapy, may consider bilevel positive airway pressure or adaptive servo-ventilation (ASV) as second-line therapy. Bilevel positive airway pressure devices have two pressure settings, one for inhalation and one for exhalation. ASV uses both inspiratory and expiratory pressure, and titrates the pressure to maintain adequate air movement. However, a clinical trial reported increased cardiovascular mortality with ASV in patients with CSA due to HF and with an ejection fraction <45%, and therefore, ASV is not recommended for this group.

For patients with hypoventilation-related CSA, first-line therapy is bilevel positive airway pressure.

Pharmacologic therapy with a respiratory stimulant may be recommended to patients with hyperventilation or hypoventilation CSA who do not benefit from positive airway pressure devices, though close monitoring is necessary due to the potential for adverse effects such as rapid heart rate, high blood pressure, and panic attacks.
Table 1: Description of Positive Airway Pressure Devices

<table>
<thead>
<tr>
<th>Device</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPAP</td>
<td>continuous positive airway pressure</td>
<td>Considered first line therapy for patients with hyperventilation-related CSA.</td>
</tr>
<tr>
<td>BPAP</td>
<td>bilevel positive airway pressure (2 pressure settings - 1 for inhalation and 1 for exhalation)</td>
<td>Considered first line therapy for patients with hypoventilation-related CSA</td>
</tr>
<tr>
<td>ASV</td>
<td>adaptive servo-ventilation (titrates the inspiratory and expiratory pressure)</td>
<td>Not recommended for patients with CSA with heart failure and left ventricular ejection fraction ≤45%</td>
</tr>
</tbody>
</table>

**Phrenic Nerve Stimulation**

Currently, there is one phrenic nerve stimulation device approved by the Food and Drug Administration, the remede System (Respicardia, Inc.). The remede System is an implantable device that stimulates the phrenic nerve in the chest which sends signals to the diaphragm to restore a normal breathing pattern. A cardiologist implants the battery-powered device under the skin in the right or left pectoral region. The procedure is conducted using local anesthesia. The device has two leads, one to stimulate a phrenic nerve (either the left pericardiophrenic or right brachiocephalic vein) and one to sense breathing. The device runs on an algorithm that activates automatically at night when the patient is in a sleeping position and suspends therapy when the patient sits up. Patient-specific changes in programming can be conducted externally by a programmer.

**Summary of Evidence**

For individuals with CSA who receive phrenic nerve stimulation, the evidence includes one randomized controlled trial (RCT) and observational studies. The relevant outcomes are change in disease status, functional outcomes, and quality of life (QOL). The RCT compared the use of phrenic nerve stimulation to no treatment among patients with CSA of various etiologies. All patients received implantation of the phrenic nerve stimulation system, with activation of the system after 1 month in the intervention group and activation after 6 months in the control group. Activation is delayed one month after implantation to allow for lead healing. At 6 months follow-up, the patients with the activated device experienced significant improvements in several sleep metrics and QOL measures. At 12 months follow-up, patients in the activated device arm showed sustained significant improvements from baseline in sleep metrics and QOL. A subgroup analysis of patients with HF combined 6-month and 12-month data from patients in the intervention group and 12-month and 18-month data from the control group. Results from
this subgroup analyses showed significant improvements in sleep metrics and QOL at 12 months compared with baseline. Results from observational studies supported the results of the RCT. No RCTs were identified in which phrenic nerve stimulation was compared with the current standard of care, positive airway pressure or respiratory stimulant medication. The evidence is insufficient to determine the effects of the technology on health outcomes.

**Ongoing and Unpublished Clinical Trials**

A currently ongoing trial that might influence this review is listed in Table 2.

**Table 2. Summary of Key Trials**

<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>NCT03238937 Treatment of Central Sleep Apnea in Patients with Heart Failure with a Cervically Implanted Phrenic Nerve Stimulator</td>
<td>40</td>
<td>Jul 2022</td>
</tr>
</tbody>
</table>

NCT: national clinical trial

**Practice Guidelines and Position Statements**

**American Academy of Sleep Medicine**

The American Academy of Sleep Medicine (2012) published a guideline on the treatment of central sleep apnea (CSA), based on results of a literature review and meta-analysis. Moderate evidence supported the use of continuous positive airway pressure or adaptive servo-ventilation to treat CSA related to congestive heart failure. Limited evidence was available for the use of positive airway pressure therapy (continuous positive airway pressure, bilevel positive airway pressure, adaptive servo-ventilation) to treat primary CSA; however, there is potential for ameliorating central respiratory events, risks are low, and the therapies are readily available. The use of phrenic nerve stimulation devices was not discussed in the guideline. An update to the guideline, published in 2016, adjusted the previous guideline, to warn that adaptive servo-ventilation is not recommended for individuals with CSA related to congestive heart failure with
ejection fraction <45%. The use of phrenic nerve stimulation as a treatment option was not addressed in the guideline.

**Medicare National Coverage**

There is no national coverage determination.

**Regulatory Status**

In October 2017, the Food and Drug Administration granted approval for the remede System (Respicardia, Inc; Minnetonka, MN) through the premarket approval application process. The approved indication is for treatment of moderate to severe CSA in adults. Product code: PSR.

**References**


### History

<table>
<thead>
<tr>
<th>Date</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>08/01/19</td>
<td>New policy, approved July 9, 2019, effective November 1, 2019. New policy created with literature review through April 2019. The use of phrenic nerve stimulation for central sleep apnea is considered investigational in all situations.</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. CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). ©2019 Premera All Rights Reserved.

**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 AppealsDepartmentquiries@Premera.com

You can file a grievance in person or by mail, fax, or email. If you need help filing 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 S09F, HHH Building
Washington, D.C. 20201, 1-800-368-1019, 800-537-7697 (TDD)

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):
يحيى هذا الإشعار معلومات هامة. قد يحيى هذا الإشعار معلومات مهمة يخصك أو شخص آخر في عائلتك. قد تكون هناك تأثيرات غير متوقعة من هذه المعلومات، وتخفيض عن تخطيطك الصحي أو السلامة.

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

中文 (Chinese):
本通知有重要的讯息。本通知可能有关於您透过 Premera Blue Cross 提交的申请或保险的重要讯息。本通知内可能有重要日期。您可能需要在截止日期之前採取行動。保留您的健康保險或者費用補貼。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).

Italiano (Italian):
Questo avviso contiene informazioni importanti. Questo avviso può contenere informazioni importanti sulla tua domanda o copertura attraverso Premera Blue Cross. Potrebbero esserci date chiave in questo avviso. Potrebbe essere necessario un tuo intervento entro una scadenza determinata per consentirti di mantenere la tua copertura o sovvenzione. Hai il diritto di ottenere queste informazioni e assistenza nella tua lingua gratuitamente.
Chiamata 800-722-1471 (TTY: 800-842-5357).
Japanese (Japanese):
この通報には重要な情報が含まれています。この通報には、Premera Blue Crossの申請または補償に関する重要な情報が含まれている場合があります。この通報に記載されている情報が正しいものであることをご確認ください。健康保険カードや保険カードを維持するには、定期的に申請したり定期的に行動を忘れないでください。

한국어 (Korean):
본 통지서에는 중요한 정보가 들어 있습니다. 즉 이 통지서는 귀하의 신청에 따라서 Premera Blue Cross 카드의 정보에 관한 정보를 포함하고 있을 수 있습니다. 본 통지서에는 각각이 되는 당신의 정보가 있을 수 있습니다。
귀하의 카드가 도난 또는 침해를 받지 않도록 하기 위해서 몇 개의 마법으로 보호해 주어야 할 필요가 있을 것입니다。
귀하의 이러한 정보와 동료 귀하의 안전을 위해 보호 방안이 없을 수 있는 권리가 있습니다. 800-722-1471 (TTY: 800-842-5357)로 문의해 주십시오.

Polski (Polish):

Português (Portuguese):

Română (Romanian):

Русский (Russian):
Настоящее уведомление содержит важную информацию. Это уведомление может содержать важную информацию о вашем заявлении или страховом покрытии через Premera Blue Cross. В настоящем уведомлении могут быть ключевые даты. Вам, возможно, потребуется принять меры к определенным предельным срокам для сохранения страхового покрытия или помощи с расходами.
Вы имеете право на бесплатное получение этой информации и помощь на вашем языке. Звоните по телефону 800-722-1471 (TTY: 800-842-5357).

Español (Spanish):
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 claras 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).

Tagalog (Tagalog):

ไทย (Thai):
ประกาศนี้มีข้อสำคัญที่เกี่ยวข้องกับการขอข้อมูลหรือการขอความช่วยเหลือของคุณผ่าน Premera Blue Cross และคุณมีสิทธิ์ในการรับข้อมูลที่คุณควรจะต้องดูในกรณีที่มีข้อกำหนดที่ระบุไว้ที่จะทำให้การขอข้อมูลหรือการขอความช่วยเหลือที่มีการแจ้งให้ทราบข้อมูลที่สำคัญและรายละเอียดที่เกี่ยวกับการบริการที่มีการแจ้งให้ทราบ โปรดติดต่อ Premera Blue Cross ที่ 800-722-1471 (TTY: 800-842-5357).

Український (Ukrainian):
Це повідомлення містить важливу інформацію. Це повідомлення може містити важливу інформацію про Ваше звернення щодо страхувального покриття через Premera Blue Cross. Зверніться у нас на адресу клієнтів, які можуть бути вказані у цьому повідомленні. Існує імовірність того, що Вам треба буде здійснити певні кроки у конкретній ситуації для того, щоб зберегти Ваше медичне страхування або отримати фінансову допомогу. У Вас є право на отримання цієї інформації та допомоги безкоштовно на Вашій рідній мові. Дозвоніться за номером телефону 800-722-1471 (TTY: 800-842-5357).

Tiếng Việt (Vietnamese):

Tilgren (Farsi):
این اطلاعیه به‌خصوص شرکت‌های مدیریت اطلاعات می‌باشد. این اطلاعیه چرا تمامی بهترین اطلاعات مربوط به فرم تاریخی، زمان بازگردانی، روش و راه‌حل‌ها، مراحل مطرح‌کردن، بازگردانی و تحلیل فرم و نحوه حفظ اطلاعات به زبان فارسی می‌باشد. این اطلاعیه به‌خوبی توضیح کاملی از مشابهیت‌های اطلاعات و کمک‌های را به دست جمعیت اطلاعات دیوانه می‌دهد. (800-842-5357).