Clinical Policy Title: Phrenic (diaphragmatic) nerve stimulation

Clinical Policy Number: 07.02.02

Effective Date: December 1, 2013
Initial Review Date: June 19, 2013
Most Recent Review Date: May 1, 2018
Next Review Date: May 2019

Related policies:
None.

ABOUT THIS POLICY: Select Health of South Carolina has developed clinical policies to assist with making coverage determinations. Select Health of South Carolina’s clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by Select Health of South Carolina when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state and federal laws and/or regulatory requirements shall control. Select Health of South Carolina’s clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. Select Health of South Carolina’s clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, Select Health of South Carolina will update its clinical policies as necessary. Select Health of South Carolina’s clinical policies are not guarantees of payment.

Coverage policy

Select Health of South Carolina considers the use of phrenic (diaphragmatic) nerve stimulation to be clinically proven with a U.S. Food and Drug Administration (FDA) approved device, such as NeuRx DPS™ RA/4 Respiratory Stimulation System (Synapse Biomedical Inc., Oberlin, Ohio), and, therefore, medically necessary for individuals 18 years and older whose remaining phrenic nerve, lung, and diaphragm function can accommodate electrical stimulation when the following criteria are met (Hayes 2016, Forleo 2015, Hirschfeld):

- The phrenic nerve stimulation is used as an alternative to invasive mechanical ventilation in cases of severe chronic respiratory failure due to cervical cord or brain lesions.
- The individual has ventilator failure due to central alveolar hypoventilation syndrome or a stable high spinal cord injury.

When either of the above criteria is met, all of these criteria also apply:

- The stimulation of the phrenic nerve (diaphragm) produces muscle activity to facilitate independent, non-ventilator-assisted breathing.
- The movement of the diaphragm is visible with fluoroscopy.
• The individual has a normal level of consciousness and normal chest anatomy.
• The individual is able to participate in and complete the education, training, and rehabilitation necessary for the appropriate use of the phrenic nerve stimulation device.

Select Health of South Carolina considers the use of phrenic (diaphragmatic) nerve stimulation to be unproven, and not medically necessary for any of the following:
• Individuals who are capable of breathing spontaneously for four or more continuous hours.
• Individuals with insufficient phrenic nerve or diaphragmatic function, causing an inability to accommodate electrical stimulation.
• Individuals with cervical spinal cord trauma that does not allow pacing or damaged cell bodies of the phrenic nerve.
• Any disease of the lower motor neurons or anterior horn cell that does not permit pacing (e.g., amyotrophic lateral sclerosis, polio myelitis).

Limitations:

All other uses of phrenic (diaphragmatic) nerve stimulation are not medically necessary. Significant nerve injury may occur during the surgical implantation procedure that may cause the phrenic nerve stimulator to be of no use to the individual. Consequently, it is possible for such a device to be indicated, but, due to nerve injury sustained during implantation, the device fails to assist the patient, resulting in a return to the use of mechanical ventilation.

Alternative covered services:

• Mechanical ventilation.

Background

The diaphragm plays a significant role in the respiratory process. It is innervated by the phrenic nerves that rely on the motor neurons of the (C3-5) cervical vertebrae, and most of its innervation comes from the C4 neurological segment. Spinal cord injury between the C0 and C4 vertebrae causes quadriplegia and may disrupt respirations, leading to the need for lifelong ventilatory support. The viability of the phrenic nerves may be assessed by electrical stimulation at the neck, and the use of fluoroscopy, a method that detects diaphragmatic movement. A phrenic nerve stimulator device, also known as a diaphragmatic pacemaker, provides electrical stimulation of the phrenic nerve to rhythmically contract the diaphragm and produce breathing in individuals who have hypoventilation. The device improves pulmonary function and may reduce the incidence of pulmonary infection. The goal of treatment with a diaphragmatic pacemaker is to free the individual from dependence on a ventilator.

The phrenic nerve stimulator has several components: an electrode(s) array is surgically implanted around the phrenic nerve(s), a radiofrequency receiver is usually implanted in the chest wall, and an
external transmitter sends radiofrequency signals to the device. The transmitter is set to send signals to stimulate the phrenic nerve to mimic normal respiratory frequencies. Intact phrenic nerves and working diaphragm muscles are essential for a phrenic nerve stimulator to function and produce the desired therapeutic effect. Any nerve damage that occurs during the surgical procedure for implantation, if sufficient, may cause the device to be of no use to the individual. Thus, there is the possibility for a phrenic nerve stimulator to be indicated for an individual, be implanted and, due to nerve trauma sustained during the implant procedure, cause the device to fail to assist the individual, resulting in the need to use mechanical ventilation.

Phrenic nerve stimulators have been used successfully to treat hypoventilation caused by a variety of conditions, including respiratory paralysis resulting from lesions of the brain stem, cervical spinal cord disruptions, and chronic pulmonary disease with ventilatory insufficiency. This device is indicated for individuals who are ventilator-dependent, those lacking the voluntary control of their diaphragm musculature to enable independent breathing without the assistance of a mechanical ventilator for at least four continuous hours a day.

Peer-reviewed professional literature supports the use of a phrenic nerve stimulator for individuals with high cervical spine injury who have an intact functioning phrenic nerve, as confirmed by electromyographic (EMG) response of the diaphragm to nerve stimulation (NHS April 2013). Randomized controlled trials for the use of a phrenic nerve stimulator are limited, due to the small number of individuals suitable for phrenic nerve stimulators and the similar number of facilities that perform the thoracic or cervical approach implantation procedure. High-quality evidence was presented in a nonrandomized trial (Hirschfeld 2008). The study compared 32 individuals treated with phrenic nerve stimulation to a similar number of participants maintained on mechanical ventilation as they were ineligible for phrenic nerve stimulation. Both groups had similar level spinal injuries. Apart from their ages and phrenic nerve statuses, the two groups were thought to be similar enough for a valid comparison. One of the best outcomes of this study was the impact of phrenic pacing on the reduction of respiratory infection.

Khong, et al. (2010) reviewed the data involving 19 individuals treated with phrenic nerve stimulation. Of these individuals, one had congenital central hypoventilation syndrome (CHHS), one had brainstem encephalitis, and 14 were quadriplegic. The total duration of the pacing ranged from one to 21 years, with eight of the 19 subjects needing revision surgeries for older pacing systems. The data review suggested that phrenic nerve stimulation could be used instead of mechanical ventilators for ongoing, long-term respiratory support.

A clinical trial (clinicaltrials.gov, ID #NCT01385384) for “Diaphragmatic Pacemaker in Tetraplegic Patients with Spinal Cord Injuries” has been conducted with the intent to use the mechanical energy of an individual’s diaphragm, with the potential that he or she may not need the ventilator tubing, tracheostomy, or — with the help of caregivers — the inconvenient mechanical ventilators. The primary outcome measure was a volume comparison of the basal with the tidal volume obtained with a diaphragmatic pacemaker over one year.
Individuals with primary alveolar hypoventilation syndrome have normal alveolar-arterial oxygen gradients and are able to voluntarily hyperventilate and normalize their PaCO2; however, they do not take enough breaths per minute. Central alveolar hypoventilation (CAH) may be genetic, known as congenital CHHS or idiopathic (acquired). The underlying cause is an abnormal integration of (autonomic) afferent signals that causes hypoventilation. For individuals with CHHS, the apnea or central hypoventilation occurs while the individual is asleep and may require tracheostomies and mechanical ventilation through his or her lifetime. A thorough clinical evaluation that includes neuromuscular tests, genetic testing, and neurological imaging may be indicated. Early diagnosis and positive pressure ventilation are essential therapeutic strategies. Phrenic nerve stimulation or pacing has been noted to benefit individuals diagnosed with alveolar hypoventilation syndromes. Treatment with the most appropriate type of ventilatory support requires referral to specialized centers with experience in diaphragm pacing.

Searches

Select Health of South Carolina searched PubMed and the following databases:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality guideline clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

We conducted searches on March 26, 2018. Search terms were: “phrenic” and “nerve stimulation.”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews**.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

Findings

Several different devices for phrenic nerve pacing have been developed. Many of the reported studies are level 4 case series or pre-post study designs looking at the feasibility of phrenic nerve stimulation devices. Long-term partial or total independence from mechanical ventilation can generally be interpreted as a successful intervention with these devices.
Further studies are necessary with phrenic (diaphragm) pacing to determine its effectiveness for the treatment of the central hypoventilation syndrome in other clinical indications and other populations, especially pediatric individuals.

**Policy updates:**

During the past twelve months there has been no further information published regarding phrenic (diaphragmatic) nerve stimulation.

Hayes notes there is insufficient published evidence to assess the safety and/or impact on health outcomes or patient management for the use of phrenic nerve stimulation for central sleep apnea.

**Summary of clinical evidence:**

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
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</thead>
</table>
| Hayes Inc. (2016) | **Key points:**
| Phrenic nerve stimulation for central sleep apnea. | • Hayes notes there is insufficient published evidence to assess the safety and/or impact on health outcomes or patient management for the use of phrenic nerve stimulation for central sleep apnea. |
| Forleo, et al. (2015) | **Key points:**
| Comparison of cardiac resynchronization therapy patients with quadripolar and bipolar left ventricular lead: | • 39 months, 418 patients, unipolar versus bipolar leads.  
• 4.6% and 14.2% had phrenic nerve stimulation (quadripolar and bipolar).  
• 100% and 84% were resolved noninvasively (quadripolar and bipolar).  
• Quadripolar leads have lower rates of problems, few phrenic nerve stimulation often not needed. |
| Hirschfeld, et al. (2008) | **Key points:**
| Phrenic nerve stimulation — controlled trials | • Population: 64 SCI subjects who were primarily mechanically ventilated through tracheostomy; 32 were treated with phrenic nerve stimulation (PNS) and 32 were mechanically ventilated (MV) over 20 years.  
• Treatment: MV or PNS.  
• Outcome measures: incidence of respiratory infections (RIs), measured in RIs per 100 days.  
• Outcome:  
  – Incidence of RI was equal in the 120 days prior to use of final respiratory device (1.43 in PNS group and 1.33 in MV group).  
  – Following use of PNS, the incidence of RI was 0 for the PNS group.  
  – Following the use of MV, the incidence of RI was 0.14 for MV group.  
  – Higher numbers of patients on PNS returned to work or school compared to MV group (9 versus 2). |
References

Professional society guidelines/other:


Peer-reviewed references:


**CMS National Coverage Determinations (NCDs):**


**Local Coverage Determinations (LCDs):**

No LCDs identified as of the writing of this policy.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill in accordance with those manuals.

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<td>Revision or removal of peripheral neurostimulator electrodes</td>
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<td>64590</td>
<td>Insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling</td>
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<td>Revision or removal of peripheral or gastric neurostimulator pulse generator or receiver</td>
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<td>Idiopathic sleep related nonobstructive alveolar hypoventilation</td>
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