Phrenic (diaphragmatic) nerve stimulation

Clinical Policy ID: CCP.1041

Recent review date: 6/2025

Next review date: 10/2026

Policy contains: Central sleep apnea; diaphragm pacing; hypoventilation; phrenic nerve stimulation.

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Coverage policy

Phrenic nerve (diaphragmatic) stimulation is clinically proven and, therefore, may be medically necessary for the treatment of chronic hypoventilation, when implanted and managed by providers with expertise in phrenic nerve/diaphragm pacing and all of the following criteria are met (Perez, 2016; Trang, 2020; U.S. Food and Drug Administration, 2001, 2008):

- Either:
  - The Avery Breathing Pacemaker® (Avery Biomedical Devices Inc., Commack, New York) for adult and pediatric members with high cervical spinal cord injury or congenital central hypoventilation syndrome.
  - The NeuRx RA/4 Diaphragm Pacing System® (Synapse Biomedical Inc., Oberlin, Ohio) for members age 18 or older with high cervical spinal cord injury.
- The member meets all of the following criteria:
  - Cannot breathe spontaneously for more than four continuous hours without mechanical ventilation.
  - The phrenic nerves and diaphragm have sufficient function to accommodate electrical stimulation.
  - The member has relatively mild or no lung disease.

Diaphragm pacers may be used with bipolar cardiac pacemakers (Perez, 2016).

Limitations

All other uses of phrenic (diaphragmatic) nerve stimulation, including treatment of central sleep apnea or amyotrophic lateral sclerosis, are investigational/not clinically proven and, therefore, not medically necessary (Luni, 2020; Orr, 2021; Voigt, 2020; Woo, 2020).

Relative contraindications include (Perez, 2016; Trang, 2020):

- Presence of active infection.
- Chronic lung disease.
- Obstructive sleep apnea.
- Need for magnetic resonance imaging.
- Ability to breathe spontaneously for four continuous hours or more without a mechanical ventilator.
- Temporary respiratory insufficiency.
- Severe behavioral disorders.
- Obesity with excess fat tissue that can impair electrical signal transfer.

Alternative covered services

- Guideline-directed medical therapy.
- Positive airway pressure (e.g., mechanical ventilation and noninvasive respiratory assist devices).
- Oxygen therapy.

Background

Hypoventilation (a.k.a. respiratory depression or hypoventilation syndrome) is the inadequate exchange of carbon dioxide and oxygen within the lungs, creating abnormal retention of carbon dioxide in the blood. It is usually secondary to other medical problems and, if left untreated, can cause significant morbidity and become life threatening. A variety of conditions can cause hypoventilation, including conditions causing diaphragmatic dysfunction (Perez, 2016; Vashisht, 2022).

Both invasive and noninvasive mechanical ventilation can assist patients with diaphragmatic dysfunction to maintain adequate ventilation. Invasive ventilation requires a tracheostomy, and both ventilator types can restrict activity participation and speech. Diaphragmatic stimulation, also known as pacing, is an alternative to mechanical ventilation for improving hypoventilation and potentially quality of life (Perez, 2016).

Diaphragmatic pacing stimulates the diaphragm to contract and relax enabling the patient to breathe without mechanical ventilation. There are two types of diaphragmatic pacers (Vashisht, 2022):

- Diaphragmatic/phrenic nerve pacing systems involve electrodes surgically attached to the phrenic nerves at the cervical, thoracic, or diaphragmatic level. Pacing wires connect the electrodes to a receiver placed under the skin. An external transmitter, serving as the main control unit, is placed above the receiver on the surface of the skin and emits radiofrequency signals.
- Diaphragmatic pacing systems provide direct stimulation to the diaphragm through four electrodes laparoscopically implanted in the diaphragm (intramuscularly) and a fifth grounding electrode implanted under the skin. An electrode connector groups the five electrodes that exit the skin into a socket called an external pulse generator.

Respiratory rates are set in the transmitter. Surgical implantation is done under general anesthesia usually in an outpatient setting, and the equipment is tested during surgery. Approximately six to eight weeks after the procedure, when surgical incisions heal, diaphragm pacing starts. Initial pacing lasts 60 to 90 minutes per night, as diaphragms tire. By three months after surgery, as the diaphragm strengthens, patients achieve the maximum

of about eight to 12 hours each day. As 24-hour pacing is not recommended due to diaphragm fatigue, some may require another method of support such as home mechanical ventilation by tracheostomy or noninvasive positive pressure ventilation (Perez, 2016).

The Avery Breathing Pacemaker received initial U.S. Food and Drug Administration premarket approval as the Mark IV transmitter in March 1998, later renamed the Spirit transmitter, for phrenic nerve stimulation after approval and use in European nations (Avery Biomedical Devices, Inc., 2023). Transmitters are surgically attached to the phrenic nerve using a cervical or thoracic approach. It is indicated for patients (no age restriction) who require chronic ventilatory support because of upper motor neuron respiratory muscle paralysis or central alveolar hypoventilation, and whose remaining phrenic nerve, lung, and diaphragm function is sufficient to accommodate electrical stimulation (U.S. Food and Drug Administration, 2001).

The NeuRx DPS RA/4 Diaphragm Pacing System received a Humanitarian Device Exemption in June 2008 for patients age 18 years or older who have stable, high spinal cord injuries and diaphragms that can be stimulated, but who lack control of them (U.S. Food and Drug Administration, 2008). In 2011, they expanded the exemption to patients age 21 years or older with amyotrophic lateral sclerosis with stimulable hemidiaphragms who experience chronic hypoventilation that has not progressed to a forced vital capacity less than 45% of predicted (U.S. Food and Drug Administration, 2011a). The NeuRx system is implanted intramuscularly via a laparoscopic procedure.

In October 2017, the U.S. Food and Drug Administration issued premarket approval to the remedē® System (Respicardia, Minnetonka, Minnesota) for treatment of moderate-to-severe central sleep apnea in nonpregnant, adult patients. Remedē consists of an implantable pulse generator and transvenous leads that monitor the patient's respiratory signals and provide unilateral electrical stimulation to the left or right phrenic nerve (U.S. Food and Drug Administration, 2017). In 2023, the remedē® System received approval for use with 1.5T and 3T magnetic resonance imaging (U.S. Food and Drug Administration, 2023).

Findings

Clinical Guidelines

Clinical guidelines offer conditional support for phrenic nerve or diaphragmatic stimulation, primarily for patients with congenital central hypoventilation syndrome or high cervical spinal cord injury. The American Thoracic Society recommends this approach for carefully selected individuals to enhance ventilation, decrease reliance on mechanical ventilators, and potentially eliminate the need for a tracheostomy, thereby improving quality of life. Potential complications, including surgical challenges, device malfunctions, and airway muscle desynchronization, require meticulous patient selection and ongoing management (Perez, 2016). Similarly, the European Congenital Central Hypoventilation Syndrome Consortium supports diaphragmatic pacing for patients over one year old who need extensive ventilatory support, noting better outcomes with tracheostomy-assisted pacing in younger children (Trang, 2020).

In 2024, the National Institute for Health and Care Excellence issued updated guidance (IPG790) on interventional procedures, endorsing phrenic nerve pacing for lifelong ventilatory support in patients with congenital central hypoventilation syndrome. This method can eliminate the need for tracheostomy or mask ventilation, improving mobility and quality of life. The guidance highlights the importance of multidisciplinary care for effective condition management but acknowledges that evidence is limited, relying on retrospective case series and database analyses. It emphasizes cautious patient selection, regular device monitoring, and awareness of potential complications, such as phrenic nerve damage or the need for device revisions (National Institute for Health and Care Excellence, 2024). This marks a shift from earlier guidance, which recommended intramuscular diaphragmatic stimulation only in research settings due to concerns about efficacy and safety (National Institute for Health and Care Excellence, 2017, 2023).

Systematic Reviews and Meta-Analyses

Systematic reviews and meta-analyses provide insights into the efficacy and safety of diaphragmatic pacing, generally supporting its benefits but noting significant evidence gaps. A systematic review found diaphragmatic stimulation effective and safe for achieving ventilator independence in 40% to 72% of ventilator-dependent patients with high cervical spinal cord injury, though manageable complications like capnothorax were common (Garara, 2016). Another review confirmed these findings but highlighted poor study quality, concluding that evidence was insufficient for a robust meta-analysis (Sieg, 2016). For patients with amyotrophic lateral sclerosis or spinal cord injury, systematic evaluations suggest inadequate evidence to broadly recommend diaphragmatic pacing due to inconsistent safety outcomes and limited benefits (Woo, 2020).

A 2025 systematic review of 10 case reports in Japan further supports diaphragmatic pacing for ventilator-dependent patients with spinal cord injury or congenital central hypoventilation syndrome (Yamauchi, 2025). All patients achieved partial or complete ventilator weaning, with 27% attaining full independence, alongside enhanced quality of life, mobility, and social reintegration. Reported complications included respiratory muscle fatigue (54%), ventilatory challenges in seated positions (18%), and stimulation-related pain (9%). The review identified barriers to adoption in Japan, such as delayed initiation (median 24 months post-injury), limited interdisciplinary collaboration, and inadequate home care support. Recommendations included early intervention, structured follow-up, and telemedicine to improve outcomes, though the small sample size and reliance on case reports limit generalizability. These reviews collectively underscore the potential of diaphragmatic pacing but call for higher-quality studies and standardized guidelines to optimize its clinical use.

Recent meta-analyses and randomized controlled trials examining transvenous phrenic nerve stimulation, particularly the remedē system for central sleep apnea in heart failure patients, provide stronger evidence. Studies show significant reductions in apnea-hypopnea indices and central apnea episodes, with improvements in sleep quality, daytime alertness, and overall quality of life (Costanzo, 2018; Iftikhar, 2022; Wang, 2023). However, limitations such as overlapping study populations and lack of long-term data persist, prompting calls for larger, independent randomized trials (Sagalow, 2022; Wang, 2023).

A 2024 systematic review and meta-analysis by Arango-Cortes and colleagues related to (n = 852) patients with diaphragmatic dysfunction, compared diaphragm pacing to mechanical ventilation and revealed disease-specific outcomes. For individuals with spinal cord injury, diaphragm electrical stimulation reduced hospital stays and respiratory infections while maintaining comparable quality of life. In contrast, for individuals with amyotrophic lateral sclerosis, diaphragm pacing was linked to higher mortality without quality-of-life benefits. These findings suggest that the effectiveness of respiratory neurostimulation depends on the underlying condition, reinforcing the need for careful patient selection.

Other Evidence

Observational studies complement these findings, highlighting high procedural success rates and manageable complication profiles. A study of individuals with cervical spinal cord injury showed that diaphragmatic pacing significantly shortened hospital stays and reduced mortality compared to standard care (Kerwin, 2018). Similarly, pivotal trials for central sleep apnea in heart failure participants reported a 97% implantation success rate and low rates of serious adverse events at six months (Augostini, 2019; Baumert, 2023a, 2023b; Hartmann, 2024; Hill, 2023).

In 2025, we reorganized and condensed the findings section and added new studies (Arango-Cortes, 2024; Yamauchi, 2025) and a revised guideline from the National Institute for Health and Care Excellence issued in 2024.

References

On May 16, 2025, we searched PubMed and the databases of the Cochrane Library, the U.K. National Health Services Centre for Reviews and Dissemination, the Agency for Healthcare Research and Quality, and the Centers for Medicare & Medicaid Services. Search terms were “phrenic nerve” (MeSH), “diaphragm” (MeSH), “electrical stimulation” (MeSH), “sleep apnea, central/therapy” (MeSH), and “phrenic nerve stimulation.” We included the best available evidence according to established evidence hierarchies (typically systematic reviews, meta-analyses, and full economic analyses, where available) and professional guidelines based on such evidence and clinical expertise.

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Policy updates

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