Medical Coverage Policy

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Diaphragmatic/Phrenic Nerve Stimulation

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benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

This Coverage Policy addresses diaphragmatic/phrenic (D/P) nerve stimulation and diaphragm pacing systems. D/P pacing is the electrical stimulation of the diaphragm via the phrenic nerve, the major nerve supply to the diaphragm that controls breathing.

Coverage Policy

Diaphragmatic/phrenic (D/P) nerve stimulation with the Avery Diaphragm Pacing System (previously the Mark IV™ Breathing Pacemaker System) as an alternative to invasive mechanical ventilation is considered medically necessary for an individual with severe, chronic respiratory failure requiring mechanical ventilation for EITHER of the following:

- alveolar hypoventilation, either primary or secondary to a brainstem disorder
- interruption of neuronal conduction at the upper cervical level, at or above the C3 vertebral level

AND when ALL of the following criteria are met:

- There is integrity of the intrathoracic section of the phrenic nerve.
- Diaphragmatic function is sufficient to accommodate chronic stimulation.
- Baseline estimated pulmonary function test is known, or likely, to be adequate.
- Individual has normal chest anatomy, normal level of consciousness, and the ability to participate in and complete the training and rehabilitation associated with the use of the device.

The NeuRx DPS® RA/4 Respiratory Stimulation System is considered medically necessary when provided in accordance with the Humanitarian Device Exemption (HDE) specifications of the U.S. Food and Drug Administration (FDA) and the individual meets ALL of the following criteria:

- Age 18 years and older
- Has a stable, high spinal cord injury
- Has a stimulable diaphragm (but lacks control of the diaphragm)

Diaphragmatic/phrenic (D/P) nerve stimulation is considered not medically necessary for ANY other indication, including but not limited to:

- **central sleep apnea**
- **amyotrophic lateral sclerosis (ALS)**
- **temporary respiratory insufficiency**
- **temporary use in difficult to wean individuals**

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

General Background

Diaphragmatic/Phrenic Nerve Stimulators for Ventilator-Dependent Conditions

Patients with high-level, C1-C3 spinal cord injuries typically experience respiratory muscle paralysis leading to chronic ventilatory insufficiency. The standard therapy for these patients is chronic mechanical ventilation via tracheostomy. Diaphragmatic/phrenic (D/P) nerve stimulation is an alternative to mechanical ventilation for a select subgroup of patients. D/P nerve stimulation is also referred to as diaphragmatic/phrenic (D/P) nerve pacing, phrenic pacing, phrenic nerve stimulation, diaphragm pacing, or electrophrenic respiration. "An implanted diaphragmatic/phrenic nerve stimulator is a device that provides electrical stimulation of a patient's phrenic nerve to contract the diaphragm rhythmically and produce breathing in patients who have hypoventilation (a state in which an abnormally low amount of air enters the lungs) caused by brain stem disease, high cervical spinal cord injury, or chronic lung disease. The stimulator consists of an implanted receiver with electrodes that are placed around the patient's phrenic nerve and an external transmitter for transmitting the stimulating pulses across the patient's skin to the implanted receiver" (U.S. Food and Drug Administration [FDA], 2023).

The two FDA approved D/P pacing systems are the Avery Diaphragm Pacing System previously known as the Mark IV™ Breathing Pacemaker System (Avery Biomedical Device, Inc., Commack, NY) and the NeuRx DPS® RA/4 Respiratory Stimulation System (Synapse Biomedical Inc., Oberlin, OH). Prior to implantation, patients may undergo diaphragm electromyography (EMG), pulmonary function studies and/or polysomnography (i.e., sleep study).

Avery Diaphragm Pacing System previously known as the Mark IV™ Breathing Pacemaker System

The Avery Diaphragm Pacing (Mark IV) system is connected to the phrenic nerve via surgically implanted receivers and electrodes in the neck or chest area (i.e., thoracotomy) which are connected to an external transmitter. Implantation is indicated in patients with alveolar hypoventilation due to primary or secondary brainstem disorders or interruption of neuronal conduction at or above the C3 vertebral level. Diagnoses of patients who may be candidates for Avery Diaphragm Pacing (Mark IV) pacing include: complete or incomplete quadriplegia, congenital central hypoventilation syndrome (i.e., Ondine's curse), diaphragmatic paralysis, central sleep apnea, brainstem stroke, brain tumor, brain injury or Arnold-Chiari malformation.

For Avery Diaphragm Pacemaker (Mark IV) pacing to be effective, candidates must have an intact phrenic nerve, a functional diaphragm, normal chest anatomy, and uncompromised lung function. The patient should be alert, mentally competent, motivated and able to complete the training and rehabilitation needed for a successful outcome.

U.S. Food and Drug Administration (FDA): The Avery Diaphragm Pacing (Mark IV ™ Breathing Pacemaker) System (Avery Biomedical Devices, Inc.) is approved by the FDA premarket approval (PMA) process as a Class III neurologic therapeutic device. The device is indicated "for persons who require chronic ventilatory support because of upper motor neuron respiratory muscle paralysis (RMP) or because of central alveolar hypoventilation (CAH) and whose remaining phrenic nerve, lung, and diaphragm function is sufficient to accommodate electrical stimulation" (FDA, 2000).

Literature Review: Nonrandomized comparative studies, prospective case series and retrospective reviews have reported that the Mark IV device is a safe and effective alternative to invasive mechanical ventilation and is considered an established alternative therapy in appropriate candidates. Clinical trials with up to ten years follow-up reported success rates of 73%–94% and included adult and pediatric patients with spinal cord injuries, congenital central alveolar hypoventilation syndrome and other causes of respiratory failure (Hirschfeld, et al., 2008; Elefteriades, et al., 2002; Shaul, et al., 2002; Garrido-Garcia, et al., 1998).

NeuRx DPS® RA/4 Respiratory Stimulation System

The NeuRx system is laparoscopically connected at the phrenic nerve motor point region in the diaphragm (i.e., intramuscular diaphragm pacing, direct pacing, or laparoscopic D/P pacing). This approach avoids the need for cervical or thoracic access to the phrenic nerve and the potential risk of phrenic nerve damage. The repetitive electrical stimulus by the pacer produces a rhythmic contraction of the diaphragm and a normal breathing pattern (i.e., inhalation upon electrical stimulation and exhalation on cessation of stimulation). The system includes four electrodes implanted in the diaphragm, a fifth electrode that completes the electrical circuit, a cable and an external pulse generator. Diaphragm stimulation devices are intended to lessen dependence on mechanical ventilators, increase mobility and independence, improve speech and sense of taste and smell, and reduce secretions and risks of infection. The NeuRx system has been proposed in patients with stable, high spinal cord injuries and in amyotrophic lateral sclerosis (ALS) patients with a stimulatable diaphragm.

Spinal Cord Injury

U.S. Food and Drug Administration (FDA): In June 2008, the NeuRx DPS® RA/4 Respiratory Stimulation System (Synapse Biomedical) received FDA approval under the Humanitarian Device Exemption (HDE) process for patients' age 18 years and older. The device is "intended for use in patients with stable, high spinal cord injuries with stimulatable diaphragms, but lack control of their diaphragms. The device is indicated to allow the patients to breathe without the assistance of a mechanical ventilator for at least 4 continuous hours a day" (FDA, 2008).

Literature Review Spinal Cord Injury: As the FDA approval for the NeuRx DPS® RA/4 Respiratory Stimulation System is an HDE, it is unlikely that there will be a sufficient body of evidence to conclusively demonstrate the safety and efficacy of this device. The available studies in the peer-reviewed published scientific literature are primarily in the form of case series and retrospective reviews. The studies (n=10-50) reported that a majority of the ventilatory dependant patients with spinal cord injuries were successfully transitioned to and paced with the NeuRx device from at least four hours and some patients up to 24 hours of the day. The available studies are limited by lack of a control or comparator group, small sample size, quality of life outcomes and long-term follow-up (Posluszny, et al., 2014, Onders, et al., 2009a; Alshekhlee, et al., 2008; Onders, et al., 2007).

FDA HDE approval of the NeuRx device was based on a prospective, non-randomized, multicenter clinical trial (FDA Summary of Safety and Probable Benefit [SBSS], 2008; Onders, et al., 2009a). A total of 50 patients were enrolled in this study at five investigational sites beginning in the year 2000. Patients in this study group have all suffered from high spinal cord injury and were full-time

dependent on positive pressure mechanical ventilation prior to enrollment. The age of enrolled patients was from 18-74 years of age. The primary endpoint was to assess the ability of the NeuRx device to provide clinically acceptable tidal volume for at least four continuous hours of pacing. The safety endpoint was to qualitatively assess the adverse event reports and compare these to a similar patient population. Secondary endpoints include reduction of dependence on mechanical ventilation and surgical implementation site independence.

Inclusion criteria:

- age 18 years or older;
- cervical spinal cord injury with dependence on mechanical ventilation;
- clinically stable following acute spinal cord injury;
- bilateral phrenic nerve function clinically acceptable as demonstrated with EMG recordings and nerve conduction times;
- diaphragm movement with stimulation visible under fluoroscopy;
- clinically acceptable oxygenation on room air (greater than 90% 02 saturation);
- hemodynamically stable;
- no medical co-morbidities that would interfere with the proper placement or function of the device;
- committed primary caregiver;
- negative pregnancy test in females of child-bearing potential;
- informed consent from the device user or designated representative.

Exclusion criteria:

- co-morbid medical conditions that preclude surgery;
- active lung disease (obstructive, restrictive or membrane diseases);
- active cardiovascular disease or active brain disease;
- hemodynamic instability or low oxygen levels on room air;
- hospitalization for or a treated active infection, within the last 3 months;
- significant scoliosis or chest deformity;
- marked obesity;
- anticipated poor compliance with protocol by either the device user or primary caregiver;
- currently breastfeeding.

The authors reported average follow-up of 2.0±1.5 years (median 1.6 years, range 0.5–8.0 years). Overall, a total of 48 out of 50 patients enrolled were able to pace for longer than four consecutive hours while achieving tidal volumes greater than their basal metabolic requirements. At the end of the study period, a total of 44 patients were actively using the device for an unspecified period of time. About 50% of the patients had used the device for more than 24 continuous hours. Five deaths, which do not appear to be device-related, were reported during the study. Two deaths occurred during mechanical ventilation, and two deaths occurred during intramuscular diaphragm stimulation. One patient lost consciousness while the stimulator was functioning, and a second patient on the stimulator died of septic shock due to urosepsis. One patient was not able to be paced. There were eleven incidents of aspiration and three incidents of upper airway obstruction that occurred in three patients. Use of the device for periods greater than four continuous hours a day occurred after a period of diaphragmatic conditioning that ranged from one week to several months.

The most frequent reported adverse event attributable to this device was capnothorax. A total of 42% of the patients enrolled in the clinical study experienced this complication in association with implantation of the electrodes in the diaphragm. While no patients experienced compromised

pulmonary gas exchange or hemodynamic instability as a result of the capnothorax, affected patients required treatment with a chest tube, for up to two days in one patient, and an extended hospital stay of five days, in one patient. The manufacturer addressed this risk in the labeling and training procedure provided with this device. This study did not report quality of life outcomes such as mobility, speech, comfort levels, and sense of taste and smell. This study lacked a control or comparator group.

Amyotrophic Lateral Sclerosis (ALS)

U.S. Food and Drug Administration (FDA): In September 2011, the NeuRx DPS® RA/4 Respiratory Stimulation System received FDA approval under the HDE process (H100006) for patients age 21 years and older. The device is "indicated for use in amyotrophic lateral sclerosis (ALS) patients with a stimulatable diaphragm (both right and left portions) as demonstrated by voluntary contraction or phrenic nerve conduction studies, and who are experiencing chronic hypoventilation (CH), but not progressed to an FVC < 45% predicted". According to the FDA Summary of Safety and Probable Benefit, data from one unpublished trial was considered in the HDE approval process. The NeuRx Diaphragm Pacing Stimulation (DPS™) System of Motor-Point Stimulation for Conditioning the Diaphragm of Patients with Amyotrophic Lateral Sclerosis (ALS) trial was a prospective study at nine clinical centers in the U.S. and France. The study enrolled 144 patients. A total of 106 patients were implanted with the DPS therapy between 2005 and 2009. The primary outcome measure was predicted forced vital capacity (FVC) to 30% of normal, by approximately 12 months. According to the FDA summary, this HDE was not taken to a meeting of the Neurological Devices Advisory Panel because it was determined that the preclinical and clinical issues raised by the HDE did not require panel review for the proposed indication." The FDA summary reported that "the Center for Devices and Radiological Health (CDRH) has determined that based on the data submitted in the HDE, that the NeuRx DPS, Diaphragm Pacing System will not expose patients to an unreasonable or significant risk or illness or injury, and the probable benefit to health from using the device outweighs the risks of illness or injury, and issued an approval order on September 28, 2011" (FDA, 2011).

The HDE post-approval study of NeuRx Diaphragm Pacing System (DPS) for Amyotrophic Lateral Sclerosis (ALS) can be found at clinicaltrials.gov identifier NCT01605006.

Literature Review ALS: The available studies in the peer-reviewed published scientific literature are primarily in the form of randomized controlled trials, systematic reviews, and prospective reviews. The randomized control trials have reported no benefit and potential harm (Marion, 2023). The studies are limited by the small, heterogeneous patient populations (n=2–74) and lack of a control or comparison group. The clinical effectiveness and long-term safety of diaphragm pacing in ALS needs to be assessed (Woo, et al., 2020; Gonzalez-Bermejo, et al., 2016; FDA, 2011; Onders, et al., 2009a; 2009b).

Woo et al. (2020) performed a systematic review of two randomized controlled trials; three case series; two case reports; one retrospective cohort study; and two prospective, non-randomized, multicenter, interventional trials (n=289) to assess the safety and efficacy of diaphragm pacing systems (DPS) for patients with respiratory failure resulting from amyotrophic lateral sclerosis (ALS) or cervical spinal cord injury (SCI). Five studies evaluated patients with ALS (n=1–74), four studies evaluated patients with either acute or chronic SCI (n=3–19), and one study evaluated patients with either ALS (n=38) or SCI (n= 50). Studies targeting ALS and SCI; using DPS as the intervention and sham or mechanical ventilation as the comparator; and outcomes focused on mortality, ventilator weaning, duration of self-respiration after operation, quality of life, operation time, hospital days, and improvement in respiration were included. Studies were excluded if they had involvement of animal or preclinical experiments, non-original articles, involvement of a system other than DPS, or an implantation approach other than laparoscopic. The intervention for all studies was DPS. The comparator for the ALS studies was either sham (n=1), mechanical

ventilation (n=1), or did not have comparator data available (n=3). The comparator for the SCI studies was either mechanical ventilation (n=1) or did not have comparator data available (n=3). The ALS/SCI study (n=1) did not have comparator data available. Outcome measures included: mortality, ventilator weaning, duration of self-respiration after operation, quality of life, operation time, hospital days after operation, and improvement in respiration. Follow up duration ranged from 1–7 years. Data reported in the ALS studies demonstrated that 78% of patients in the intervention groups experienced a complication compared to 3% in the control groups. There was no improvement in the quality of life for the intervention group compared to the control group and patients in the intervention group had a shorter survival than those in the control group. One study in the SCI review reported capnothorax in 42% of procedures. Differences in overall survival was not seen between the intervention groups compared to the control groups. Ventilator weaning was achieved in 33% of patients in a pediatric case series and 96% of patients in an adult prospective cohort study. Adverse events reported in the ALS studies included but was not limited to: pneumothorax, capnothorax, ARDS, venous thromboembolism, and respiratory failure. Author noted limitations included: lack of high quality studies and the small number of studies included in the review. Additional limitations noted include: small patient populations, lack of a control for several of the studies, and heterogeneous patient populations.

The DiPALS Writing Committee (2015) conducted a multicenter, open-label, randomized controlled trial to assess the safety and efficacy of diaphragm pacing with the NeuRX RA/4 Diaphragm Pacing System in patients with amyotrophic lateral sclerosis (ALS). Patients (n=74) 18 and older were included if they had probable or definite ALS, had been stable on riluzole treatment for 30 days or longer, had been diagnosed with respiratory insufficiency, and had intact bilateral phrenic nerve function. Exclusion criteria were: previous use of non-invasive ventilation, a pre-existing implanted electrical device, cardiac or pulmonary disease, pregnancy or breastfeeding, inability to perform decision-making, obesity, scoliosis or chest wall deformity, diaphragm abnormality, or forced vital capacity of <50% predicted or sniff test of < 30cm H20. The intervention (n=37) was non-invasive ventilation plus diaphragm pacing. Patients were asked to set a one month pacing target of 30 minutes per day, five times a day. During the second month, patients were asked to gradually lengthen the sessions. Non-invasive ventilation alone (n=37) with a target of four hours or longer overnight and daytime use if clinically required served as the comparator. The primary outcome measured was overall survival defined as time from randomization to death. Secondary outcomes measured included: patient quality of life, care giver quality of life, tolerability, and adverse events. Follow-up occurred at two, three, six, nine, and 12 months after randomization. Following recommendations from the Data Monitoring and Ethics Committee (DMEC), recruitment was suspended two years and 14 days after it began due to concerns over survival data. Participants already enrolled continued in the study for another six months and 6 days at which time another recommendation was given by the DMEC to discontinue pacing in all patients. The intervention group experienced significantly shorter overall median survival rates of 11 months compared to 22.5 months in the comparator group (p=0.009). Seventy-six percent of patients died in the pacing group compared to 51% in the comparator group. There were a reported 162 adverse events in the intervention group compared to 81 in the comparator group. These events included but were not limited to: respiratory complication (e.g., chest infection, decompensated respiratory failure, pneumothorax), pain, infection of PEG or PIG, wire problems, cardiovascular system complications, and death. Causes of death were reported as respiratory failure, chest infection, ALS, and hyperthermia. The authors noted the un-masked design of the study as a limitation and a possible opportunity for bias. Additional limitations of the study included the small sample size.

Gonzalez-Bermejo et al. (2016) conducted a multicenter, randomized, controlled, triple-blinded trial to assess whether early diaphragm pacing would prolong diaphragm functionality thereby delaying the need for non-invasive ventilation. Patients (n=74) ranged in age from 49–66 years. Patients greater than 18 years were included if they had probable or definitive ALS, sitting forced

vital capacity of 60–80%, and a documented response of the diaphragm to diagnostic phrenic nerve stimulation. Patients were excluded if they had: an indication for non-invasive ventilation at the time of screening, an underlying respiratory disease other than ALS affecting pulmonary function, previous non-invasive ventilation or CPAP, comorbidities that would increase the risk of anesthesia or reduce survival, obesity or chest deformity potentially making electrode placement difficult, diaphragmatic hernia, respiratory tract infection in the previous two months, presence of a cardiac pacemaker or defibrillator, pregnancy or breastfeeding, or participation in any other clinical trial that could possibly affect the safety or outcome of the study. All patients underwent laparoscopic placement of intradiaphragmatic electrodes. Patients were then randomly allocated to receive either an active (n=37) or non-active (n=37) cable. The initial target for pacing sessions was five times per day with each session lasting a minimum of 30 minutes. Ten days after the initiation of therapy, patients were asked to lengthen the pacing sessions and to reduce the number of sessions in an effort to achieve one continuous session lasting more than three hours. Sham served as the comparator. The primary outcome measured was the duration of time a patient remained free from non-invasive ventilation calculated from the time of randomization to the initiation of non-invasive ventilation or death. Secondary outcomes measured included: duration of time a patient remained free from non-invasive ventilation calculated from the onset of ALS symptoms, overall tracheostomy-free survival from randomization and onset of symptoms, quality of life, quality of sleep, tolerability, and adverse events. Follow up occurred every three months. Data published in the DiPALS study prompted the safety committee to preemptively analyze the data according to group allocation after 33 months and 12 days resulting in an interim un-masking to assess survival. Significant mortality was noted in the active stimulation group compared to the comparator (p=0.026) and therefore, the study was terminated with 49 patients remaining alive at the time of termination. Eighteen deaths were observed in the active treatment group compared to seven in the sham stimulation group. Patients in the active group achieved non-invasive ventilation-free survival for six months on average compared to 8.8 months in the sham group (p=0.02). Serious, non-fatal adverse events included: capnothorax, pneumothorax, acute respiratory failure, venous thromboembolism, gastrostomy, and organ lesion during surgery. Causes of death included: chest infection (44%), other cause of respiratory failure (28%) and palliative care (28%). Author noted limitations included: difficulty in masking treatment allocation from the patients given that the intervention resulted stimulation-related movements and pain; possible allocation bias by an external, masked committee; and heterogeneous patient populations. An additional limitation of the study is the small patient population.

Onders et al. (2009a) prospectively evaluated the complete worldwide multi-center experience with diaphragm pacing stimulation (DPS) to maintain and provide diaphragm function in ventilator-dependent spinal cord injury (SCI) patients and respiratory-compromised patients with amyotrophic lateral sclerosis (ALS). The study results for the SCI patients have been documented in the spinal cord injury literature review of the Coverage Policy. This study was undertaken under FDA Investigational Device Exemption (IDE). Each site's Institutional Review Board (IRB) approved the study. The studies were registered at clinicaltrials.gov with the specific identifiers NCT00010374 and NCT00420719. The ALS patients being reported were involved in three separate IRB trials under the same IDE with some overlap of the trials. After surgical implantation and diaphragm conditioning the patients were followed with the same tests every 4–12 weeks until the 1-year time period ended. The tests over the course of the trial for these patients included the Short Form 36 (SF-36), Revised Amyotrophic Lateral Sclerosis Functional Rating Scale (ALSFR-R) scoring, phrenic nerve studies, diaphragm ultrasound thickness, fluoroscopic sniff tests, pulmonary function tests, arterial blood gases, laboratory tests, and electrode characterizations including electromyographic assessments. Continuous positive airway pressure (CPAP) or noninvasive positive pressure ventilation (NIPPV) may still be needed to maintain an upper airway and was used in conjunction with DPS. From March of 2000 to September of 2007, a total of 38 ALS patients were implanted with DPS using the NeuRx device at five centers. The age of the patients at implantation ranged from 18-74 years. Patients with ALS had much weaker

diaphragms identified surgically, requiring trains of stimulation during mapping to identify the motor point at times. There was no peri-operative mortality even in ALS patients with forced vital capacity (FVC) below 50% predicted. Five patients (13%) had capnothorax secondary to air tracking above the diaphragm. It was treated with either observation or simple aspiration. The capnothoraxes caused no hemodynamic or respiratory problems. There was no cardiac involvement from diaphragm pacing even when analyzed in 10 patients who had pre-existing cardiac pacemakers. No infections occurred even with simultaneous gastrostomy tube placements for ALS patients. The authors reported that after conditioning the diaphragm with the DPS, preliminary results show an average rate of decline in FVC of 0.9% per month from the pre-implantation decline of 2.4% a month, which extrapolates to an additional 24 months of ventilator-free survival. The authors reported that this multi-center experience has shown that laparoscopic diaphragm motor point mapping, electrode implantation, and pacing can be safely performed in ALS patients and delays the need for ventilators, increasing survival. The study is limited by the small, heterogeneous patient population and lack of a control or comparison group.

Onders et al. (2009b) prospectively evaluated perioperative management (i.e., preoperative planning, intraoperative management, and immediate postoperative management) to determine the safety and efficacy of laparoscopic implantation of the NeuRx system in ALS patients. The two-center study included at total of 51 patients in three subgroups, an initial pilot trial (n=16), two patients who were implanted for compassionate reasons, and 33 additional patients implanted at a later date. A predicted forced vital capacity (FVC) above 50% at enrollment and 45% at implantation was the primary inclusion criterion. There was a 19% increase of respiratory compliance when diaphragmatic pacing was synchronized with the anesthesiology ventilator. There were no perioperative respiratory infections, failures to extubate or 30-day mortalities. The study is limited by the small, heterogeneous patient population derived from three separate groups and lack of a control or comparison group.

Professional Societies/Organizations ALS:
American College of Chest Physicians: The 2023 American College of Chest Physicians Clinical Practice Guideline and Expert Panel Report (Khan, et al., 2023) provided evidence-based recommendations for the respiratory management of patients with neuromuscular diseases (NMDs). The panel reported the evidence of best practices for respiratory management in NMD is limited and based primarily on observational data in amyotrophic lateral sclerosis. The panel did not address diaphragm pacing for the respiratory management of patients with neuromuscular diseases (NMDs).

Other Indications
D/P pacing has been proposed for respiratory support in other diagnostic conditions to delay the need for mechanical ventilation. The NeuRx has been proposed for patients with muscular dystrophies, polio and hypoventilation syndromes tetraplegia. However, the evidence in the published peer-reviewed scientific literature does not support the NeuRx or the Avery Diaphragm pacing system (Mark IV stimulation) systems for any other indications.

Phrenic Nerve Stimulation/Central Sleep Apnea
Central sleep apnea (CSA) is a disorder characterized by repetitive cessation or decrease of both airflow and ventilatory effort during sleep. CSA can be primary (i.e., idiopathic CSA) or secondary. Examples of secondary CSA include CSA associated with Cheyne-Stokes breathing, a medical condition, a drug or substance, or high altitude periodic breathing. CSA associated with Cheyne-Stokes breathing is particularly common among patients who have had a stroke or have heart failure. Sleep disordered breathing (SDB) is important to recognize because it is associated with adverse cardiovascular outcomes and mortality and because accumulating evidence suggests that treatment of SDB can improve heart failure-related outcomes and quality of life. Most cases of CSA are secondary to an underlying medical condition, central nervous system pathology, or

medication side effect. Treatment of the underlying condition or removal of the offending medication or substance may result in improvement. The extent to which CSA is expected to improve varies by the condition but rarely results in complete resolution. In patients with heart failure, a variety of interventions (i.e., medical therapy, cardiac resynchronization, ventricular assist devices or transplantation) have been associated with improvements in the severity of sleep apnea. However, these interventions do not lead to complete resolution of the abnormal breathing pattern and should be considered complementary to CSA-specific therapy (Badr, 2024).

Hyperventilation-related central sleep apnea (CSA) is the most common form of CSA. It includes primary CSA and CSA associated with Cheyne-Stokes breathing, a medical condition (e.g., heart failure) or high altitude periodic breathing. Continuous positive airway pressure (CPAP) is the preferred first-line therapy for symptomatic patients with hyperventilation-related CSA. Supplemental oxygen during sleep has been proposed for patients with hyperventilation-related CSA who have hypoxemia during sleep. Treatment options for patients who fail or do not tolerate CPAP depend upon the underlying etiology of the CSA and individual patient characteristics. For patients with CSA due to heart failure with reduced ejection fraction (≤45%) who do not tolerate or respond to CPAP, the optimal approach is uncertain.

A large multicenter randomized control trial, the SERVE-HF study, showed elevated all-cause and cardiovascular mortality risk in patients with central sleep apnea and symptomatic heart failure with an estimated ejection fraction of ≤45% who were randomized to adaptive servo-ventilation (ASV). Therefore, use of ASV in this patient population is not advised at the current time. Treatment options for patients with CSA and an ejection fraction >45% who fail or do not tolerate CPAP include ASV and bilevel positive airway pressure (BPAP) with a back-up respiratory rate. ASV remains an option in patients with hyperventilation-related CSA and a preserved ejection fraction, although treatment decisions in such patients are individualized, and there is a paucity of direct data in these patients. BPAP therapy is an option when used in the spontaneous timed (ST) mode (i.e., with a back-up rate) targeted to normalize the apnea-hypopnea index (AHI); it is considered for the treatment of CSA if there is no response to CPAP or oxygen therapy. At present, the use of BPAP with a back-up rate in patients with CSA due to heart failure with reduced ejection fraction is approached with caution and on a case-by-case basis. Patients who do not tolerate or benefit from positive airway pressure therapy or supplemental oxygen during sleep may benefit from treatment with a respiratory stimulant, such as acetazolamide; however, such medications can have harmful side effects and should be monitored closely (Badr, 2024; Mansukhani, et al., 2023).

Hypoventilation-related CSA is less common and includes CSA associated with central nervous system diseases, central nervous system suppressing drugs or substances (e.g., opioids), neuromuscular diseases, or severe abnormalities in pulmonary mechanics. In patients with CSA whose central apneas are due to hypoventilation, BPAP is first-line therapy. Patients may also benefit from treatment with a pharmacological respiratory stimulant but such medications can have harmful side effects and need to be monitored closely (Badr, 2024).

An alternative approach to treating patients with CSA has been investigated using unilateral, transvenous phrenic nerve stimulation to restore a physiological breathing pattern throughout sleep. This therapy stimulates the diaphragm during sleep to stabilize gas exchange and maintain normal breathing. The remedē® System (ZOLL Medical Corporation, Minnetonka, MN; formerly Respicardia, Inc., Minnetonka, MN) is a fully implanted neurostimulator intended for treatment of moderate-to-severe CSA in adults. The remedē system delivers unilateral transvenous phrenic nerve stimulation to cause diaphragmatic contraction that mimics a normal breathing pattern. The contraction of the diaphragm creates a negative intrathoracic pressure similar to that generated by normal breathing, which is intended to result in a decrease in central apneas during sleep. System components include an implantable, battery-powered pulse generator, a sensing lead, a stimulating lead and an external system programmer (FDA, 2017).

U.S. Food and Drug Administration (FDA): The remedē® System (ZOLL Medical Corporation, Minnetonka, MN; formerly Respicardia, Inc., Minnetonka, MN) received FDA premarket approval (PMA) October 2017. The device is an implantable phrenic nerve stimulator indicated for the treatment of moderate to severe central sleep apnea (CSA) in adult patients. The remedē System is contraindicated for patients with an active infection and patients known to require magnetic resonance imaging (MRI).

The FDA Summary of Safety and Effectiveness Data states there are several other alternatives for the treatment of moderate to severe central sleep apnea. Each treatment has advantages and disadvantages. A patient should fully discuss these treatment options with their physician to select the therapy that best meets expectations and lifestyle.

Treatment alternatives include:

- positive airway pressure (PAP) therapies
  - continuous positive airway pressure (CPAP)
  - bi-Level positive airway pressure (BPAP)
  - adaptive servo ventilation (ASV)
- nocturnal oxygen therapy
- medications:
  - acetazolamide
  - theophylline

Literature Review: The FDA approval of the remedē system is based on results of one pivotal, randomized, controlled trial (RCT) that compared the remedē system with sham therapy and evaluated the safety and effectiveness of unilateral neurostimulation in patients with central sleep apnea (Costanzo, et al., 2016). The multicenter trial randomly assigned 151 eligible patients to the stimulation (treatment) and optimal medical therapy (n=73) or no stimulation and optimal medical therapy (control) (n=78) groups for six months. Patients in the control group had the device implanted at time of randomization but not activated until six-month effectiveness endpoints were assessed, ending the randomized portion of the trial. Potentially eligible patients prospectively underwent a qualifying overnight stay and had a polysomnography within 40 days before implant. Eligibility required the following polysomnography results: apnea-hypopnea index (AHI) of at least 20 events per hour of sleep, central apneas at 50% or higher of all apneas, at least 30 central apnea events throughout the night, and an obstructive apnea index (OAI) of 20% or lower of the total AHI. Exclusion criteria were factors prohibitive of device implantation, phrenic nerve palsy, Stage D heart failure, a cerebrovascular event within the past 12 months, central sleep apnea secondary to opioids, and advanced renal disease (serum creatinine concentration >221 µmol/L or calculated creatinine clearance ≤30 mL/min23). Baseline demographics and clinical characteristics were similar between groups. The primary effectiveness endpoint in the intention-to-treat population was the comparison of the proportions of patients in the treatment versus control groups achieving a 50% or greater AHI reduction from baseline to six months, measured by a full-night polysomnography assessed by masked investigators in a core laboratory. The primary safety endpoint of 12-month freedom from serious adverse events related to the procedure, system, or therapy was evaluated in all patients. In the analysis of the intention-to-treat population, more patients in the treatment group (35 [51%] of 68) had an AHI reduction from baseline of 50% or greater at six months than had those in the control group (eight [11%] of 73; difference between groups 41%, 95% CI 25-54, p<0·0001). 138 (91%) of 151 patients had no serious-related adverse events at 12 months. Seven (9%) cases of related-serious adverse events occurred in the control group and six (8%) cases in the treatment group. Seven patients died unrelated to implant, system, or therapy. Twenty-seven (37%) of 73 patients in the treatment group reported non-serious therapy-related discomfort that was resolved with simple

system reprogramming in 26 (36%) patients, but was unresolved in one (1%) patient. This study is limited by the short-term follow-up.

Costanzo et al (2018a) reported the 12-month results from the remedē® System Pivotal Trial above to evaluate whether the benefits of this therapy are long-lasting. Composition of the per protocol population through the 12-month post-therapy initiation included stimulation (treatment) group n=54 and no stimulation (control) n=65. Sleep indices were assessed from baseline to 12 months in the treatment group and from six to 12 months in former controls. In the treatment group, a ≥ 50% reduction in AHI occurred in 60% of patients at six months and 67% at 12 months. After six months of therapy, 55% of former controls achieved ≥50% reduction in AHI. Patient Global Assessment was markedly or moderately improved at six and 12 months in 60% of treatment patients. Improvements persisted at 12 months. A serious adverse event within 12 months occurred in 13 patients (9%).

Fox et al. (2019) reported the long-term efficacy and safety of phrenic nerve stimulation (PNS) in patients from the remedē® System Pivotal Trial at 24 (n=109) and 36 (n=60) months. At the time of the Pivotal Trial closure, the original 151 patients had been followed for 32 ± 13 months (median=35, maximum=52 months) and 94 patients were ongoing at the time of trial closure. All patients remaining in the trial at the time of closure had completed a minimum of 24 months of follow-up; however, 33 patients had not yet reached the 36-month visit. In agreement with FDA, ongoing patients were asked to enroll into the remedē System Post Approval Study (NCT03425188). Baseline characteristics included mean age 64 years, 91% male, and mean apnea–hypopnea index (AHI) 47 events per hour. Sleep metrics (polysomnography) and echocardiographic parameters are reported at baseline, 12, 18, and 24 months, in addition to available 36-month sleep results from polygraphy. Safety was assessed through 36 months; however, analysis focused through 24 months and available 36-month results are provided. Sleep metrics (AHI, central apnea index, arousal index, oxygen desaturation index, rapid eye movement sleep) remained improved through 24 and 36 months with continuous use of PNS therapy. At least 60% of patients in the treatment group achieved at least 50% reduction in AHI through 24 months. Left ventricular ejection fraction showed small, but measurable, improvements with this therapy but whether this finding is of any clinical relevance will be a cornerstone of future clinical trials. Serious adverse events (SAEs) related to the remedē System implant procedure, device, or therapy through 24 months were reported by 10% of patients, no unanticipated adverse device effects or deaths, and all events resolved. No additional related SAEs were reported between 24 and 36 months. One limitation in the study design is that the control group was followed for only six months prior to activating therapy so the control data is limited. At the time of the study design, it was felt that depriving patients with symptomatic central sleep apnea of any treatment for longer than six months was unethical. Another limitation is that not all patients completed 36 months follow-up at the time the Pivotal Trial was closed following FDA approval. Also, additional adverse events after 24 months may be reported in the ongoing remedē System Post Approval Study (NCT03425188) that is following patients from the Pivotal Trial through five years post implant. The authors concluded that the data suggests beneficial effects of long-term PNS in patients with CSA appear to sustain through 36 months with no new safety concerns. The results of the Post Approval Study of the Remedē System (NCT03425188) have been posted to clinicaltrials.gov however, have not yet been published.

Costanzo et al (2021) reported the five year safety and efficacy results of transvenous phrenic nerve stimulation (TPNS) therapy using the remedē System for the treatment of adults with moderate to severe central sleep apnea (CSA). Due to study sites or patients declining participation, not all patients participated in this continuation study. Fifty-three of the original 151 Pivotal Trial patients consented to participate in the Post Approval Study (PAS) with 52 patients completing the five year visit. Results of the apnea-hypopnea index (AHI) decreased from a baseline median of 46 events/hour to 17/hour at five years. Similarly, the central-apnea index

(CAI) reduced from a baseline median of 23 events/hour to one/hour at five years. The mixed apnea index, obstructive apnea index and hypopnea index were unchanged through five years. Epworth Sleepiness Scale (ESS) results were clinically meaningful and improved by ≥2 points from baseline in 74% (37/50) and by ≥3 points from baseline in 62% (31/50) of patients. The heart failure subgroup analysis (n=29) at five years, AHI was reduced by a median of 25 events/hour, CAI reduced to two events/hour, the median 4% oxygen desaturation index (ODI4) improved from 41 events/hour at baseline to 20 events/hour, the median arousal index decreased from 41 events/hour at baseline to 19 events/hour, and the ESS improved from a score of eight at baseline to four. In years 3–5, four patients reported serious adverse events (SAE): one stimulation lead dislocation, two stimulation lead component failure, and one implant site infection after device replacement. There were no deaths reported in patients participating in the PAS. Study limitations include not all Pivotal Trial sites and patients chose to participate in the PAS five year follow up and lack of control group at five years.

Abraham et al. (2015) conducted a prospective, multicenter, nonrandomized study of 57 patients to evaluate chronic, transvenous, unilateral phrenic nerve stimulation to treat central sleep apnea (CSA). The patients underwent baseline polysomnography followed by transvenous phrenic nerve stimulation system implantation and follow-up. The study assessed feasibility implantation success rate and therapy delivery. Safety was evaluated by monitoring for device and procedure-related adverse events. Efficacy was evaluated by changes in the apnea-hypopnea index at three months. Quality of life at six months was evaluated using a sleepiness questionnaire, patient global assessment, and, for those with heart failure at baseline, the Minnesota Living With Heart Failure Questionnaire. The study met its primary end point, demonstrating a 55% reduction in apnea-hypopnea index from baseline to three months. Central apnea index, oxygenation, and arousals significantly improved along with favorable effects on quality of life and sleepiness were noted. In patients with heart failure, the Minnesota Living With Heart Failure Questionnaire score significantly improved. Device or procedure-related serious adverse events occurred in 26% of patients through six months post-therapy initiation, predominantly due to lead repositioning early in the study. Efficacy was maintained at six months. The authors concluded that transvenous, unilateral phrenic nerve stimulation appears safe and effective for treating CSA and that the findings should be confirmed in a prospective, randomized, controlled trial.

In a meta-analysis, Luni et al. (2020) reported whether phrenic nerve stimulation is efficacious in the treatment of central sleep apnea (CSA). A total of five studies (one randomized controlled trial [n=151] and four prospective trials [n=3-47]) were included in the meta-analysis (n=204). Follow-up was one night to four years. One study used the temporary external pulse generator system to study the acute effects of PNS while the rest used the implantable remede System. The authors reported that the pooled data demonstrated a reduction of mean apnea hypopnea index with PNS compared to controls by -26.7 events/hour. PNS causes a significant reduction of the AHI but does not eliminate CSA leaving the treatment group with the presence of mild to moderate sleep apnea. The mean difference in central apnea index was -22. The mean reduction in the oxygen desaturation index of 4% or more demonstrated a decrease in PNS group by -24.16 events/hour compared with controls. PNS resulted in mean reduction in arousal index of -13.77. The mean change in percent of time spent in rapid eye movement sleep demonstrated a nonsignificant increase in PNS group by 1.01%. PNS was safely tolerated with no deaths related to device implant. The authors concluded that PNS may be a safe and effective therapy for treating CSA especially in heart failure population. However, large randomized studies are needed to evaluate the long-term safety of PNS and any long-term effects that PNS may have on clinical outcome such as mortality and heart failure admissions.

Professional Societies/Organizations: No evidence-based clinical practice guidelines regarding the use of implantable transvenous phrenic nerve stimulation to treat central sleep apnea are available.

Temporary Respiratory Insufficiency or for Temporary Use in Difficult to Wean Patients

Patients are placed on mechanical ventilation for a variety of reasons. Patients are considered difficult-to-wean if they fail their first spontaneous breathing trial (SBT) or Ventilator Liberation Trial (VLT) and then require up to three SBTs/VLTs or seven days to pass an SBT/VLT. Up to 40 percent of patients mechanically ventilated for an acute illness in the intensive care unit (ICU) are difficult-to-wean. If repeat attempts are unsuccessful at weaning, it usually signifies incomplete resolution of the illness that precipitated mechanical ventilation and/or the development of one or more new problems that prevent weaning. These issues (eg, respiratory, cardiac, psychological, circuit, nutritional) should identified and treated before resuming further weaning trials. Respiratory muscle weakness is common among mechanically ventilated patients. It may be present at the time of intubation or result from ICU-acquired paresis or ventilator-induced respiratory muscle weakness. Respiratory muscle strength is typically evaluated by clinical examination at the bedside by asking the patient to take a maximal inspiratory effort. Respiratory muscle weakness is probable if there is weak effort or low lung volumes. Additional objective bedside measures to support clinical findings include a low negative inspiratory force (eg, <60 cm H_2O) and poor diaphragmatic excursion by ultrasound. Physical therapy is the mainstay of treatment. Inspiratory muscle strength training (IMST) is of unclear benefit and not routinely used (Epstein, 2023).

It has been proposed that stimulation of the phrenic nerves to induce diaphragmatic contractions may help strengthen the diaphragm to prevent and treat ventilator-induced diaphragm dysfunction (VIDD) and therefore assist in weaning patients off of ventilator use. The Lungpacer AeroPace™ system is one device currently being studied in clinical trials. According to the manufacturer website, "The AeroPace™ system is an investigational device and its use is limited by Federal Law and is only available for investigational use purposes" (Lungpacer Medical, 2022).

U.S. Food and Drug Administration (FDA): There are no FDA approved, licensed, or cleared device treatments to assist in weaning patients off of ventilators.

Literature Review: The available studies in the peer-reviewed published scientific literature are primarily in the form of randomized controlled trials, a feasability study, and a case report. The studies are limited by the small, heterogeneous patient populations (n=2–102) and lack of a control or comparison group. The clinical effectiveness and safety of temporary phrenic nerve stimulation or diaphragmatic pacing in difficult to wean patients needs to be assessed (Dres, et al., 2022; Keough-Delgado, et al., 2021; Ataya, et al., 2020).

Medrinal et al. (2023) conducted a randomized control trial to evaluate the effectiveness of transcutaneous electrical stimulation of the diaphragm (TEDS) in decreasing diaphragmatic dysfunction and improving respiratory muscle strength in patients in the intensive care unit (ICU). The theory was TEDS would prevent diaphragm dysfunction during the weaning process from mechanical ventilation. Sixty-six patients were randomized using a 1:1 ratio to receive either active electrical stimulation or sham stimulation daily. The primary outcome measured was ultrasound measurements of diaphragm thickening fraction (DTF) during spontaneous breathing trials. Secondary outcomes measured included maximal inspiratory muscle pressure (MIP), peak cough flow (PEF) and extubation failure. The mean loss of diaphragm thickness during mechanical ventilation did not differ between groups (p=0.99). There were no differences between the groups in respiratory muscle variables or the secondary outcomes. No adverse events were reported during the sessions. The authors concluded TEDS did not prevent diaphragm dysfunction or improve inspiratory muscle strength in mechanically ventilated patients.

Dres et al. (2022) conducted a multicenter, randomized control trial of 102 patients to evaluate the efficacy of temporary transvenous diaphragm neurostimulation (TTDN) on ventilator weaning

outcome in difficult-to-wean patients. Patients were included if they were ≥ 18 years old, had been on invasive mechanical ventilation (MV) (intubation or tracheotomy) for > 96 hours and satisfied protocol-defined readiness-to-wean criteria but had failed at least two attempts at ventilator liberation (failed spontaneous breathing trial [SBT], extubation with subsequent reintubation within 48 hours). Excluded were patients with any of the following: current extracorporeal membrane oxygenation, failed weaning from MV because of current hypervolemia as determined by the clinicians in charge, clinically overt congestive heart failure, anatomical features preventing left subclavian vein catheterization, history of congenital heart disease, current neuromuscular blockade treatment, preexisting neuromuscular disease potentially affecting respiratory muscles, pleural effusions occupying more than one third of the pleural space on either side on chest X-ray, body mass index (BMI) of >40 kg/m^2, known/suspected phrenic nerve paralysis, presence of any electrical device (implanted or external) with the potential to interact/interfere with the TTDN system, bacteremia, current hemodynamic instability (need for vasopressors), current sepsis/septic shock, terminal illness with an estimated life expectancy of six months or not committed to full care, known/suspected pregnancy, lactating, or actively participating in another clinical study pertaining to MV. The main reason for intubation was acute respiratory distress syndrome (ARDS) (35% overall) and around half the patients had a tracheostomy tube at inclusion. The mean length of time of MV before inclusion was 27 ± 18 days (treatment) and 29 ± 23 days (control). Both groups were treated according to a standardized daily weaning protocol. Patients were randomly assigned to receive stimulation (treatment group) plus the standard of care for difficult and prolonged mechanical ventilation weaning (intent-to-treat: n=57; modified intent-to-treat: n=43) or only receive standard of care for difficult and prolonged mechanical ventilation weaning (control group) (n=55). The treatment group received two to three pacing sessions per day that consisted of four sets of 10 or six sets of 10 consecutive stimulations administered manually in synchrony with the ventilator. Sessions were conducted for up to 30 days and were stopped when patients successfully passed the SBT and were extubated. The primary efficacy endpoint was the cumulative incidence of successful weaning by day 30 in both groups. Secondary efficacy endpoints included: the number of days from baseline to removal from MV as a result of successful weaning or day 30, whichever came first; reinstatements of MV by day 30; difference between groups in maximal inspiratory pressure (MIP) changes from baseline to last available measurement; change in MIP over time; rate of MIP change per day from baseline to last available measurement; 30-day survival; changes in diaphragmatic thickening fraction from baseline to last available measurement; changes in rapid shallow breathing index (RSBI); and proportion of patients requiring tracheostomy. Fourteen patients were excluded due to the guidewire not being able to be placed or the catheter or pacing therapy could not be delivered. Successful weaning from the ventilator occurred in 82% of the treatment group and in 74% of the control group. Duration of mechanical ventilation was 12.7 ± 9.9 days for treatment group and 14.1 ± 10.8 days for control group. In the treatment group, the maximal inspiratory pressure increased by 16.6 cm H_2O and by 4.8 cm H_2O in the control group. The frequency of serious adverse events was similar in both groups. Median stimulation-related pain in the treatment group was zero (no pain). Author noted study limitations included inclusion of patients who were unlikely to benefit from diaphragm pacing because of weaning failure risk factors independent of diaphragm function, heterogeneous population regarding duration of MV at baseline, unable to obtain optimal statistical power, and only 79% of the patients in the treatment group received >50% of the target number of stimulations. In conclusion, compared to standard treatment, temporary transvenous diaphragm neurostimulation did not increase the proportion of successful weaning from mechanical ventilation in patients who had been on a ventilator for almost a month.

Professional Societies/Organizations: There are no evidence-based clinical practice guidelines regarding the use of implantable transvenous phrenic nerve stimulation for use with temporary respiratory insufficiency or to assist in weaning patients off of ventilators.

Pediatric Population

Literature Review: Diaphragmatic/ phrenic nerve stimulation has been proposed in the pediatric population (i.e., individuals < 18 years of age) for a variety of conditions including tetraplegia, congenital central alveolar hypoventilation syndrome (CCAHS), cervical spinal cord injury, acute flaccid myelitis, and central neurological cause. The available studies in the peer-reviewed published scientific literature are primarily in the form of case series, case reports, and retrospective studies. The studies are limited by the small patient populations (n=6–28) and lack of a control or comparator group. The clinical effectiveness and long-term safety of diaphragmatic pacing in the pediatric population needs to be further assessed (Onders, et al., 2011; Ali, et al., 2008; Onders, et al., 2007; Shaul, et al., 2002; Garrido-Garcia, et al., 1998).

Professional Societies/Organizations:

American Thoracic Society (ATS): In their discussion of the diagnosis and management of children with congenital central hypoventilation syndrome (CCHS) (Weese-Mayer, et al., 2010) the ATS states that in a subset of children, diaphragm pacing can be used during wakefulness to allow for age-appropriate activities while receiving assisted ventilation.

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	Phrenic Nerve Stimulator/160.19	The effective date of this version has not been posted.
LCD		No Determination found	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

1. This list of codes may not be all-inclusive.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
64575	Open implantation of neurostimulator electrode array; peripheral nerve (excludes sacral nerve)
64580	Open implantation of neurostimulator electrode array; neuromuscular
64590	Insertion or replacement of peripheral, sacral, or gastric neurostimulator pulse generator or receiver, requiring pocket creation and connection between electrode array and pulse generator or receiver

HCPCS Codes	Description
C1767	Generator, neurostimulator (implantable), nonrechargeable
C1778	Lead, neurostimulator (implantable)

HCPCS Codes	Description
C1816	Receiver and/or transmitter, neurostimulator (implantable)
C1820	Generator, neurostimulator (implantable), with rechargeable battery and charging system
C1883	Adapter/Extension, pacing lead or neurostimulator lead (implantable)
C1897	Lead, neurostimulator test kit (implantable)
L8680	Implantable neurostimulator electrode, each
L8683	Radiofrequency transmitter (external) for use with implantable neurostimulator radiofrequency receiver
L8685	Implantable neurostimulator pulse generator, single array, rechargeable, includes extension
L8686	Implantable neurostimulator pulse generator, single array, non-rechargeable, includes extension
L8687	Implantable neurostimulator pulse generator, dual array, rechargeable, includes extension
L8688	Implantable neurostimulator pulse generator, dual array, non-rechargeable, includes extension
L8696	Antenna (external) for use with implantable diaphragmatic/phrenic nerve stimulation device, replacement, each

Considered Not Medically Necessary:

CPT®* Codes	Description
33276	Insertion of phrenic nerve stimulator system (pulse generator and stimulation lead(s), including vessel catheterization, all imaging guidance, and pulse generator initial analysis with diagnostic mode activation when performed
33277	Insertion of phrenic nerve stimulator transvenous sensing lead (List separately in addition to code for primary procedure)
33281	Repositioning of phrenic nerve stimulator transvenous lead(s)
33287	Removal and replacement of phrenic nerve stimulator, including vessel catheterization, all imaging guidance, and interrogation and programming, when performed; pulse generator
33288	Removal and replacement of phrenic nerve stimulator, including vessel catheterization, all imaging guidance, and interrogation and programming, when performed; transvenous stimulation or sensing lead(s)
93150	Therapy activation of implanted phrenic nerve stimulator system, including all interrogation and programming
93151	Interrogation and programming (minimum one parameter) of implanted phrenic nerve stimulator system
93152	Interrogation and programming of implanted phrenic nerve stimulator system during polysomnography
93153	Interrogation without programming of implanted phrenic nerve stimulator system
0424T	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) (Code deleted 12/31/2023)
0425T	Insertion or replacement of neurostimulator system for treatment of central sleep apnea; sensing lead only (Code deleted 12/31/2023)
0426T	Insertion or replacement of neurostimulator system for treatment of central sleep apnea; stimulation lead only (Code deleted 12/31/2023)

CPT®* Codes	Description
0427T	Insertion or replacement of neurostimulator system for treatment of central sleep apnea; pulse generator only (Code deleted 12/31/2023)
0428T	Removal of neurostimulator system for treatment of central sleep apnea; pulse generator only (Code deleted 12/31/2023)
0429T	Removal of neurostimulator system for treatment of central sleep apnea; sensing lead only (Code deleted 12/31/2023)
0430T	Removal of neurostimulator system for treatment of central sleep apnea; stimulation lead only (Code deleted 12/31/2023)
0431T	Removal and replacement of neurostimulator system for treatment of central sleep apnea, pulse generator only (Code deleted 12/31/2023)
0432T	Repositioning of neurostimulator system for treatment of central sleep apnea; stimulation lead only (Code deleted 12/31/2023)
0433T	Repositioning of neurostimulator system for treatment of central sleep apnea; sensing lead only (Code deleted 12/31/2023)
0434T	Interrogation device evaluation implanted neurostimulator pulse generator system for central sleep apnea (Code deleted 12/31/2023)
0435T	Programming device evaluation of implanted neurostimulator pulse generator system for central sleep apnea; single session (Code deleted 12/31/2023)
0436T	Programming device evaluation of implanted neurostimulator pulse generator system for central sleep apnea; during sleep study (Code deleted 12/31/2023)
0674T	Laparoscopic insertion of new or replacement of permanent implantable synchronized diaphragmatic stimulation system for augmentation of cardiac function, including an implantable pulse generator and diaphragmatic lead(s)
0675T	Laparoscopic insertion of new or replacement of diaphragmatic lead(s), permanent implantable synchronized diaphragmatic stimulation system for augmentation of cardiac function, including connection to an existing pulse generator; first lead
0676T	Laparoscopic insertion of new or replacement of diaphragmatic lead(s), permanent implantable synchronized diaphragmatic stimulation system for augmentation of cardiac function, including connection to an existing pulse generator; each additional lead (List separately in addition to code for primary procedure)
0677T	Laparoscopic repositioning of diaphragmatic lead(s), permanent implantable synchronized diaphragmatic stimulation system for augmentation of cardiac function, including connection to an existing pulse generator; first repositioned lead
0678T	Laparoscopic repositioning of diaphragmatic lead(s), permanent implantable synchronized diaphragmatic stimulation system for augmentation of cardiac function, including connection to an existing pulse generator; each additional repositioned lead (List separately in addition to code for primary procedure)
0679T	Laparoscopic removal of diaphragmatic lead(s), permanent implantable synchronized diaphragmatic stimulation system for augmentation of cardiac function
0680T	Insertion or replacement of pulse generator only, permanent implantable synchronized diaphragmatic stimulation system for augmentation of cardiac function, with connection to existing lead(s)
0681T	Relocation of pulse generator only, permanent implantable synchronized diaphragmatic stimulation system for augmentation of cardiac function, with connection to existing dual leads

CPT®* Codes	Description
0682T	Removal of pulse generator only, permanent implantable synchronized diaphragmatic stimulation system for augmentation of cardiac function
0683T	Programming device evaluation (in-person) with iterative adjustment of the implantable device to test the function of the device and select optimal permanent programmed values with analysis, review and report by a physician or other qualified health care professional, permanent implantable synchronized diaphragmatic stimulation system for augmentation of cardiac function
0684T	Peri-procedural device evaluation (in-person) and programming of device system parameters before or after a surgery, procedure, or test with analysis, review, and report by a physician or other qualified health care professional, permanent implantable synchronized diaphragmatic stimulation system for augmentation of cardiac function
0685T	Interrogation device evaluation (in-person) with analysis, review and report by a physician or other qualified health care professional, including connection, recording and disconnection per patient encounter, permanent implantable synchronized diaphragmatic stimulation system for augmentation of cardiac function

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Revision Details

Type of Revision	Summary of Changes	Date
Annual review	• No changes to coverage statement	7/15/2024
Annual review	• Updated to new template and formatting standards. • Added not covered: temporary respiratory insufficiency and in difficult to wean patients.	9/15/2023