Medical Policy

Blue Cross Blue Shield Blue Care Network of Michigan

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***Current Policy Effective Date: 11/1/24**
(See policy history boxes for previous effective dates)

Title: Phrenic Nerve Stimulation and Diaphragm Pacing

Description/Background

Respiratory insufficiency, or ventilatory failure, can be caused by a variety of conditions including spinal cord injury, central nervous system disorders, stroke, encephalitis, and pituitary dysfunction. Congenital or acquired disruption of the nervous system in the brain (medulla and/or the pons) may also cause respiratory insufficiency or ventilatory failure. The respiratory center in the medulla normally signals the diaphragm to contract, and the action of the muscles of the neck, upper chest and intercostals expand the ribcage initiating inhalation. Patients without functional respiratory centers or spinal cord lesions in the cervical spine are often dependent on mechanical ventilators or other mechanical systems to support their respiratory function. Continuous ventilatory support may be required for patients with conditions of high spinal cord injury, surgical lesion or head trauma.

Mechanical ventilation has been the most common way of supporting ventilation. Both negative and positive pressure devices have been used for many years. There are a number of mechanical ventilators available. They provide continuous or intermittent ventilatory support including positive and negative pressure devices. These types of devices restrict the patient's mobility and ability to speak. Caregivers are required to assist patients that are supported by a ventilator, which increases the cost of care.

An alternative to mechanical ventilation is phrenic nerve stimulation, also called diaphragm/phrenic nerve pacing or electrophrenic respiration. The phrenic nerve originates mainly from the fourth cervical nerve, but also receives contributions from the fifth and third cervical nerves. The phrenic nerves contain motor, sensory and sympathetic nerve fibers that provide the only motor supply to the diaphragm. Phrenic nerve pacemakers have been developed to stimulate the phrenic nerves with regular electrical pulses, causing the diaphragm muscle to contract, initiating a normal breathing process. Stimulation of the diaphragm causes the floor of the chest cavity to lower which increases negative pressure within the chest bringing air into the lungs.

Diaphragm Pacing Through Phrenic Nerve Stimulation (Mark IV™)

Cervical or Thoracic Approach
The device has an external transmitter, receivers that are surgically implanted in the chest or abdomen, and electrodes which are attached to the right and left phrenic nerves. In most cases, the electrodes are implanted in the chest; however, in the case of a structural issue or other concern, the electrodes may be placed in the neck. The transmitter sends a signal that the receiver converts to an electrical current that stimulates the phrenic nerves. This stimulation results in a contraction of the diaphragm muscles.[1]

Diaphragm Pacing by Direct Diaphragm Stimulation (NeuRx™)
Direct diaphragm stimulation involves implanting intramuscular electrodes in the diaphragm near the insertion points of the phrenic nerves. There is no direct contact with the phrenic nerve.

NeuRX Diaphragm Pacing System (DPS)™ RA/4 Respiratory Stimulation System
This device is intended for use in patients with stable, high spinal cord injuries with stimulable diaphragms, but who 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. The NeuRx Diaphragm Pacing System is intended for use in patients 18 years and older with stable high spinal cord injuries who lack control of the diaphragm but who will benefit from diaphragm stimulation to help them breathe without relying on a mechanical ventilator. The system can support patient breathing continuously for 4 or more hours each day.

Regulatory Status:

Avery phrenic nerve pacing device prototypes were brought into commercial distribution by Avery Laboratories, Inc. in the early 1970's for use. The Avery Mark IV device was FDA approved in January 1987 without a patient age restriction.[2] The Mark IV consists of electrodes that are placed in the neck or chest, an implantable receiver and a programmable transmitter that sends radio signals to the receiver. The Mark IV transmitter is worn on a belt or pocketed.

The NeuRx DPS™RA/4 Respiratory Stimulation System (Synapse Biomedical, Inc) consists of electrodes that are placed in the phrenic nerve motor point region in the diaphragm, an external stimulator (pulse generator) as well as a clinical station.[3] The electrodes are implanted and connected to the external stimulator. The clinical station is used to set up initial stimulation and sensing responses intra-operatively as well as record the diaphragm's response to the stimulation. Postoperatively, it used to optimize the amplitude, pulse width, pulse frequency, respiration rate and inspiration interval. It communicates the settings or changes to the transmitter. The NeuRX device was approved as a humanitarian device exemption (HDE) in 2008 for ventilator dependent spinal cord injury patients over the age of 18 years who lack voluntary control of their diaphragms.

On September 29, 2011, NeuRx DPS (diaphragm pacing system) received an HDE for use in patients with Amyotrophic Lateral Sclerosis (ALS).[4] The FDA approval specifies that use of the pacing system is intended for "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 (forced vital capacity) less than 45% predicted. For use only in patients 21 years of age or older."

Medical Policy Statement

The safety and effectiveness of phrenic nerve stimulation/diaphragm pacing have been established. It may be a useful therapeutic option when indicated for selected patients, using devices that have been granted full pre-market approval from the FDA.

Inclusionary and Exclusionary Guidelines

Inclusions for FDA-Approved Device (Avery Mark IV™):
Patient is at least 18 years of age, with either:

- Ventilatory failure from a stable, high spinal cord injury **or**
- Central alveolar hypoventilation syndrome

And, the following criteria are met:

- Bilateral clinically-acceptable phrenic nerve function (demonstrated with EMG recordings and nerve conduction times), AND
- Normal chest anatomy, a normal level of consciousness, and the individual has the ability to participate in and complete the training and rehabilitation associated with the use of the device, AND
- Diaphragm movement with stimulation, visible under fluoroscopy or ultrasound, AND
- Diaphragmatic/phrenic nerve stimulation allows breathing without the support of a ventilator for at least 4 continuous hours a day.

Exclusions:

- Individual who is able to breathe spontaneously for 4 continuous hours or more without use of a ventilator
- Individual with intact and functional phrenic nerve and diaphragm
- Individual whose respiratory insufficiency is temporary
- Motor neuron disease, such as amyotrophic lateral sclerosis (ALS)
- Treatment of a condition where the phrenic nerve and diaphragm are intact and functional (eg, chronic obstructive lung disease, central sleep apnea, restrictive lung disease, singultus [hiccups])
- Underlying cardiac, pulmonary or chest6 wall disease which prevents spontaneous breathing for more than 4 continuous hours, even with the use of a phrenic nerve stimulator or diaphragm pacing system

Humanitarian Device Exemption

On March 31, 2023, The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the NeuRX Diaphragm Pacing System (DPS). This device is intended for use in patients with stable, high spinal cord injuries with stimulatable diaphragms, but who 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. For use only in patients 18 years of age or older. We are pleased to inform you that the PMA P2000018 is approved.[5] The NeuRx Diagphram Pacing System is intended for use in patients 18 years and older with stable high spinal cord injuries who lack control of the diaphragm but who will benefit

from diaphragm stimulation to help them breathe without relying on a mechanical ventilator. The system can support patient breathing continuously for 4 or more hours each day.

NeuRx DPS® has been approved for distribution in the U.S. under Humanitarian Device Exemptions (HDE) H070003 for a spinal cord injury (SCI) indication and HDE H100006 for an amyotrophic lateral sclerosis (ALS) indication. The device has been distributed in Europe to treat diaphragm dysfunction which includes patients with spinal cord injury (SCI), amyotrophic lateral sclerosis (ALS), and other forms of diaphragm dysfunction under EC certificate number 518356. The device is also approved by the Pharmaceuticals and Medical Devices Agency (PMDA) in Japan. In addition, the device has been approved and distributed in Canada, Australia, Brazil, Israel, Middle East, Scandinavian countries, South Africa, Switzerland, South America, and North Africa. To date, over 2,000 NeuRx DPS® devices have been implanted world-wide. The NeuRx DPS® has not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device

In 2008, NeuRx DPS™ RA/4 received FDA approval through a humanitarian device exemption (HDE) application for use in patients 18 years of age or older who have stable, high spinal cord injuries. This application is for a medical device intended to benefit patients in the treatment of a disease or condition that affects a relatively small number of individuals in the United States per year. A HDE does not require results of scientifically valid clinical investigations on effectiveness. The FDA only requires sufficient information to determine that the device does not pose unreasonable or significant risk of illness or injury.

On September 29, 2011, NeuRx DPS™ RA/4 (diaphragm pacing system) received an HDE for use in patients 21 years of age and older with Amyotrophic Lateral Sclerosis (ALS).

Devices that carry a Humanitarian Device Exemption status are not fully approved by the FDA and are considered experimental/investigational by Blue Cross of Michigan. However, upon appeal, if the case meets FDA's established criteria, individual consideration may be extended.

CPT/HCPCS Level II Codes *(Note: The inclusion of a code in this list is not a guarantee of coverage. Please refer to the medical policy statement to determine the status of a given procedure)*

Established codes:

64575	64585	64590	64595	95972	
L8680	L8681	L8682	L8683	L8685	L8686
L8687	L8688				

Other codes (investigational, not medically necessary, etc.):

39599

Note: Individual policy criteria determine the coverage status of the CPT/HCPCS code(s) on this policy. Codes listed in this policy may have different coverage positions (such as established or experimental/investigational) in other medical policies.

Rationale

Studies in the 1970's (Glenn et al) determined phrenic nerve pacing was an option for quadriplegic patients with respiratory paralysis.[6] The authors reported results of 50 patients who received phrenic nerve pacing for quadriplegia, chronic pulmonary disease and central alveolar hypotension. Techniques were described for electrode and receiver implantation and management and selection of the pacing schedule for each group of patients, with laboratory evidence to support the clinical findings.

Creasey et al (1996) concluded that diaphragm pacing appeared to provide both health and lifestyle advantages and freedom from positive pressure ventilator by reducing risk of tracheal problems, chronic infection and other ventilator related complications.[7] By 1996 more than 1000 patients were known to have been treated with diaphragm pacing, compared to 488 in 1988.

In 2007, the Avery device was studied for use in Ondine disease, or congenital central alveolary hypoventilation syndrome(Ali et al [2002]).[8] Following insertion of the pacemaker, diaphragmatic conditioning was performed by increasing pacing time to increase the strength of the diaphragm until 12 hours of pacing was reached. All individuals in the study were either working or in school and were able to participate in sports if they chose.

Onders et al (2009) reviewed the results and differences in patients with spinal cord injuries and patients with amyotrophic lateral sclerosis when diaphragm pacing was performed.[9] Diaphragm motor point mapping and electrode placement and pacing was performed in both groups with success. Diaphragm pacing delayed the need for ventilatory and increased survival time in ALS patients. The procedure is minimally invasive and can be safely performed in an outpatient treatment setting.

Onders et al (2014), in a final analysis of a pilot trial, reported that long-term analysis of diaphragm pacing in patients with amyotrophic lateral sclerosis found no safety issues and positively influenced diaphragm physiology and survival.[10] The FDA granted an HDE based upon the results of these findings.

Phrenic nerve pacing offers several advantages over mechanical ventilation, primarily a more normal breathing pattern because of the contraction of the respiratory muscles. DiMarco et al (2009), reviewed aspects of phrenic nerve pacing, comparing mechanical ventilation, phrenic nerve pacing and normal respiratory patterns.[11] DiMarco et al also examined combined intercostal and phrenic nerve pacing for possible improvements over the pacing systems that are currently available. He concluded that combined intercostal and phrenic nerve pacing would improve inspiratory intercostal/accessory muscle activation that would contribute to improved inspiratory capacity.

Posluszny et al (2014) reported on a retrospective review of a multicenter nonrandomized protocol of laparoscopic diaphragm motor point mapping with electrode implantation for diaphragm condition and weaning from ventilator support.[12] The protocol was employed in a small population of patients (n=29) during the initial hospitalization after spinal cord injury. Seven of the 29 patients had nonstimulatable diaphragms and did not receive the implanted electrode. The remaining patients were implanted. Sixteen patients (72%) were able to wean off ventilator support in an average of 10.2 days. Of the remaining implanted patients, two had delayed weans of 180 days, three had partial weans using diaphragm pacing at times throughout the day, and one patient successfully implanted went to a long-term acute care

facility and subsequently had life prolonging measures withdrawn. Eight patients had complete recovery of respiration and diaphragm pacing wires were removed. The authors concluded that early laparoscopic diaphragm motor point mapping following spinal cord injury can identify those patients with complete phrenic motor neuron loss or injury. They observed that in patients with an intact phrenic system but lacking control of ventilation, diaphragm pacing can shorten duration of mechanical ventilation and may allow for complete independence of mechanical ventilation in certain cases.

Results from uncontrolled prospective and retrospective studies have shown that phrenic nerve/diaphragm pacing is a viable alternative for carefully selected patients who depend on mechanical ventilators. Patients who retain function of the phrenic nerves and diaphragm are considered candidates for this therapy. Phrenic nerve/diaphragm pacing offers a patient adequate respiration in select highly motivated patients and allows freedom of mobility and restoration of speech and a sense of smell over positive pressure mechanical ventilation. Phrenic nerve/diaphragm pacing can be maintained for a number of years, which allows a more normal lifestyle for patients with respiratory dysfunction and cervical spine injuries.

Government Regulations

National:

National Coverage Determination (NCD) Phrenic Nerve Stimulator (160.19). This is a longstanding national coverage determination. The effective date of this version has not been posted.

Item/Service Description

The phrenic nerve stimulator provides electrical stimulation of the 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). The device has been used successfully to treat hypoventilation caused by a variety of conditions, including respiratory paralysis resulting from lesions of the brain stem and cervical spinal cord and chronic pulmonary disease with ventilatory insufficiency. The phrenic nerve stimulator is intended to be an alternative to management of patients with respiratory insufficiency who are dependent upon the usual therapy of intermittent or permanent use of a mechanical ventilator as well as maintenance of a permanent tracheotomy stoma.

However, an implanted phrenic nerve stimulator can be effective only if the patient has an intact phrenic nerve and diaphragm. Moreover, nerve injury may occur during the surgical procedure and if sufficient injury is incurred, the device will not prove useful to the patient. Consequently, it is possible for such a device to be indicated for a patient but, due to injury sustained during implant, fail to assist the patient, resulting in a return to the use of mechanical ventilation.

The implantation of a phrenic nerve stimulator is covered for selected patients with partial or complete respiratory insufficiency.

Local:

There is no local coverage determination addressing phrenic stimulation or diaphragm pacing.

(The above Medicare information is current as of the review date for this policy. However, the coverage issues and policies maintained by the Centers for Medicare & Medicare Services [CMS, formerly HCFA] are updated

and/or revised periodically. Therefore, the most current CMS information may not be contained in this document. For the most current information, the reader should contact an official Medicare source.)

Related Policies

- Phrenic Nerve Stimulation for Central Sleep Apnea
- Obstructive Sleep Apnea and Snoring - Surgical Treatment
- Positive Pressure Airway Devices
- Diagnosis of Sleep Disorders
- Ventilators and Accessories, BCN Only (Retired)

References

1. American Thoracic Society, Diaphragm Pacing by Phrenic Nerve Stimulation. https://www.thoracic.org/patients/patient-resources/resources/diaphragm-pacing-online.pdf Accessed 5/9/24.
2. U. S. Food and Drug Administration (FDA), Department of Health and Human Services. Premarket Approval for the Avery Breathing Pacemaker System Mark IV™ (Avery Biomedical Device, Inc., Commack, NY), P860026 http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_template.cfm?id=p860026 Accessed 5/9/24.
3. U. S. Food and Drug Administration (FDA), Department of Health and Human Services. NeuRx DPSTM, RA/4 Respiratory Stimulation System H070003, June 17, 2008 http://www.accessdata.fda.gov/cdrh_docs/pdf7/H070003b.pdf Accessed 5/9/24.
4. U. S. Food and Drug Administration (FDA), Department of Health and Human Services. NeuRx DPS, Diaphragm pacing System H100006, September 28, 2011 http://www.accessdata.fda.gov/cdrh_docs/pdf10/h100006a.pdf Accessed 5/9/24.
5. U. S. Food and Drug Administration (FDA), Department of Health and Human Services. NeuRX Diaphragm Pacing System (DPS) P200018. March 31, 2023 Correspondence Generator (CorGen) (fda.gov)accessed 5/9/24.
6. Glenn W, et al. Long-term ventilatory support by diaphragm pacing in quadriplegia. Annals of Surgery. 1976, Vol. 183, No. 5, pp. 566-577.
7. Creasey G, et al. Electrical stimulation to restore respiration. Journal of Rehabilitation and Research and Development. 1996, Vol. 33, No. 2, pp. 123-132.
8. Ali A, et al. Diaphragmatic pacing for the treatment of congenital central alveolar hypoventilation syndrome. Journal of Pediatric Surgery. 2008, Vol. 43, pp. 792-796.
9. Onders R, et al. Complete worldwide operative experience in laparoscopic diaphragm pacing: Results and differences in spinal cord injured patients and amyotrophic lateral sclerosis patients. Surgical Endoscopy. 2009, Vol. 23, No. 7, pp. 1433-1440.
10. Onders RP, et al. Final analysis of the pilot trial of diaphragm pacing in amyotrophic lateral sclerosis with long-term follow-up: diaphragm pacing positively affects diaphragm respiration. Am J Surg. 2014, Vol. 207, No. 3, pp. 393-397.
11. DiMarco A, Phrenic nerve stimulation in patients with spinal cord injuries. Respiratory Physiology and Neurobiology, 2009, Vol. 169, pp. 200-209.
12. Posluszny JA, et al. Multicenter review of diaphragm pacing in spinal cord injury: successful not only in weaning from ventilators but also in bridging to independent respiration. J Trauma Acute Care Surg. 2014, Vol. 76, No. 2, pp. 303-310.

13. Centers for Medicare & Medicaid Services (CMS). Medicare Coverage Database. Phrenic Nerve Stimulator. Manual Section Number 160.19.

The articles reviewed in this research include those obtained in an Internet based literature search for relevant medical references through 5/9/24, the date the research was completed.

Joint BCBSM/BCN Medical Policy History

Policy Effective Date	BCBSM Signature Date	BCN Signature Date	Comments
3/1/11	2/17/11	1/4/11	Joint policy established
5/1/12	2/21/12	2/21/12	Routine maintenance
11/1/12	8/21/12	8/21/12	Routine maintenance, CPT code 64577 deleted. Added CPT code 64575.
3/1/15	12/12/14	12/29/14	Routine maintenance
7/1/16	4/19/16	4/19/16	Routine maintenance Added CPT codes 0424T-0436T Added “stimulation” to policy title Added central sleep apnea to the list of exclusions
7/1/17	4/18/17	4/18/17	Routine maintenance
7/1/18	4/17/18	4/17/18	Routine maintenance
7/1/19	4/16/19		Routine maintenance Rationale, references and government regulations information updated
11/1/19	9/30/19		Updates to inclusions / exclusions; government regulations.
11/1/20	8/18/20		Routine maintenance Removed codes, description and rationale related to central sleep apnea and the remedē System. Ref 19 added.
11/1/21	8/17/21		Routine maintenance
5/1/22	3/11/22		Codes added: 64585, 64590, 64595, 95972 One inclusion edited. HDE statement revised.
11/1/22	8/16/22		Routine maintenance (ls)
11/1/23	8/15/23		Routine maintenance (jf) Vendor Managed: NA Added ref: 5

3/1/24	12/19/23		• 2024 Annual CPT Update (jf) • Nomenclature revisions to codes 64590 and 64595 • Vendor Managed: NA
11/1/24	8/20/24		Routine maintenance (jf) Vendor Managed: NA

Next Review Date: 3rd Qtr, 2025

BLUE CARE NETWORK BENEFIT COVERAGE
POLICY: PHRENIC NERVE STIMULATION AND DIAPHRAGM PACING

I. Coverage Determination:

Commercial HMO (includes Self-Funded groups unless otherwise specified)	Covered, criteria apply
BCNA (Medicare Advantage)	See Government Regulations section.
BCN65 (Medicare Complementary)	Coinsurance covered if primary Medicare covers the service.

II. Administrative Guidelines:

- The member's contract must be active at the time the service is rendered.
- Coverage is based on each member's certificate and is not guaranteed. Please consult the individual member's certificate for details. Additional information regarding coverage or benefits may also be obtained through customer or provider inquiry services at BCN.
- The service must be authorized by the member's PCP except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Services must be performed by a BCN-contracted provider, if available, except for Self-Referral Option (SRO) members seeking Tier 2 coverage.
- Payment is based on BCN payment rules, individual certificate and certificate riders.
- Appropriate copayments will apply. Refer to certificate and applicable riders for detailed information.
- CPT - HCPCS codes are used for descriptive purposes only and are not a guarantee of coverage.