



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

Subject **Diaphragmatic/Phrenic Nerve Stimulation**

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Hyperlink to Related Coverage Policies

- Electromyography Studies
- Noninvasive Negative Pressure Ventilators
- Ventilator Weaning

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health 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. Proprietary information of CIGNA. Copyright ©2011 CIGNA

Coverage Policy

CIGNA covers diaphragmatic/phrenic (D/P) nerve stimulation with the Mark IV™ Breathing Pacemaker System as an alternative to invasive mechanical ventilation as 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.

CIGNA covers the NeuRx DPS™ RA/4 Respiratory Stimulation System as medically necessary for an individual age 18 years or older with a stable, high spinal cord injury and a stimlatable diaphragm when provided in accordance with the Humanitarian Device Exemption (HDE) specifications of the U.S. Food and Drug Administration (FDA).

CIGNA does not cover D/P stimulation for ANY other indication, including amyotrophic lateral sclerosis (ALS), because it is considered experimental, investigational or unproven.

General Background

Patients with high-level, vertebrae 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 pacing is an alternative to mechanical ventilation for a select subgroup of patients.

D/P pacing, also referred to as phrenic pacing, phrenic nerve stimulation, diaphragm pacing, or electrophrenic respiration, is the electrical stimulation of the diaphragm via the phrenic nerve, the major nerve supply to the diaphragm that controls breathing. The two FDA approved D/P pacing systems are 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). These systems are an established alternative for a defined subset of patients who require ventilatory assistance. Prior to implantation, patients may undergo diaphragm electromyography (EMG), pulmonary function studies and/or polysomnography (i.e., sleep study).

Mark IV™ Breathing Pacemaker System

The Mark IV system is connected to the phrenic nerve by electrodes in the neck or chest area (i.e. thoracotomy approach). The device consists of surgically implanted receivers and electrodes 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 the upper cervical level, at or above the C3 vertebral level. Diagnoses of patients who may be candidates for 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. Candidates for NeuRx DPS include patients with spinal cord injuries from automobile accidents, falls, trauma, sports injuries or disease (e.g., polio, and spinal bifida).

For 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 Mark IV™ Breathing Pacemaker System 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 potential risks 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.

U.S. Food and Drug Administration (FDA): The NeuRx DPS™ RA/4 Respiratory Stimulation System is FDA approved under the Humanitarian Device Exemption 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: As the FDA approval for the NeuRx device is an HDE, it is unlikely that there will be a sufficient body of evidence to conclusively demonstrate the safety and efficacy of this method. The available studies are primarily in the form of case series and retrospective reviews and reported that ventilatory dependant patients with spinal cord injuries were successfully transitioned to and paced with the NeuRx device for up to 24 hours of the day (Onders, et al., Jul 2009; Alsheklee, et al., 2008; Onders, et al., 2007).

ECRI conducted a systematic review of the literature on NeuRx DPS and reported that one prospective, observational study (n=50) with a mean 1.7 years follow-up met inclusion criteria. The study did not include a quality of life assessment measuring the impact of NeuRx on mobility, speech, comfort level and sense of taste and smell. No comparative studies were found and outcome consistency could not be assessed.

In an Issues in Emerging Health Technologies report regarding laparoscopic diaphragm pacing for tetraplegia (i.e., NeuRx), the Canadian Agency for Drugs and Technologies in Health (2009) reported that there were “no evidence-based recommendations regarding appropriate strategies for ventilator support” for this patient population. The published data is comprised of prospective studies with a mean follow-up of 1.7 years. Long-term effects are unknown, and data comparing the NeuRx to existing pacing systems are lacking.

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, hypoventilation syndromes, tetraplegia and amyotrophic lateral sclerosis (ALS or Lou Gehrig’s disease). However, the evidence in the published peer-reviewed scientific literature does not support the NeuRx or the Mark IV stimulation systems for any other indications.

Literature Review: Onders et al. (Mar 2009) 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. A predicted forced vital capacity (FVC) above 50% at enrollment and 45% at implantation was the primary inclusion criterion. The two-center study included 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. 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

American Thoracic Society (ATS): In their discussion of the diagnosis and management of children with congenital central hypoventilation syndrome (CCHS), ATS (2009) stated that D/P pacing is one form of chronic ventilation at home that is an option for children with CCHS. D/P pacing allows for increased mobility and improved quality of life.

National Institute for Health and Clinical Excellence (NICE): In a guidance document on intramuscular diaphragm stimulation as an alternative for phrenic nerve stimulation using implanted electrodes in the neck or chest for ventilator-dependent patients with chronic respiratory failure, NICE (2009) (United Kingdom), stated that although the evidence “raises no major safety concerns”, “current evidence on its efficacy is inadequate to quantify”. Studies included patients with spinal cord injury and ALS.

Summary

Evidence in the published peer-reviewed scientific literature and professional societies support diaphragmatic/phrenic (D/P) nerve stimulation with the Mark IV™ Breathing Pacemaker for a subgroup of individuals with chronic respiratory failure requiring mechanical ventilation. Under the Humanitarian Device Exemption (HDE) specifications of the U.S. Food and Drug Administration (FDA) the NeuRx DPS™ RA/4

Respiratory Stimulation System is indicated for a subgroup of individuals with stable, high spinal cord injuries. There is insufficient evidence to support D/P nerve stimulation by either device for the treatment of all other indications including amyotrophic lateral sclerosis (ALS).

Coding/Billing Information

Note: This list of codes may not be all-inclusive.

Covered when medically necessary:

CPT®* Codes	Description
64577	Incision for implantation of neurostimulator electrodes; autonomic nerve
64590	Insertion or replacement of peripheral or gastric neurostimulator pulse generator or receiver, direct or inductive coupling

HCPCS Codes	Description
L8680	Implantable neurostimulator electrode, each
L8681	Patient programmer (external) for use with implantable programmable neurostimulator pulse generator
L8682	Implantable neurostimulator radiofrequency receiver
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

ICD-9-CM Diagnosis Codes	Description
327.24†	Idiopathic sleep related nonobstructive alveolar hypoventilation
327.25†	Congenital central alveolar hypoventilation syndrome
344.01	Quadriplegia and quadriparesis, C1-C4, complete
344.02	Quadriplegia and quadriparesis, C1-C4, incomplete
518.83	Chronic respiratory failure
V46.11	Dependence on respirator, status

†**Note:** Covered when medically necessary and used to report diaphragmatic/phrenic (D/P) nerve stimulation with the Mark IV™ Breathing Pacemaker System.

Experimental/Investigational/Unproven/Not Covered:

ICD-9-CM Diagnosis Codes	Description
045.00- 045.93	Acute poliomyelitis
138	Late effects of acute poliomyelitis
335.20	Amyotrophic lateral sclerosis

344.00	Quadriplegia unspecified
359.0-359.29	Muscular dystrophies and other myopathies
359.3	Periodic paralysis

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References

1. Alshekhlee A, Onders RP, Syed TU, Elmo M, Katirji B. Phrenic nerve conduction studies in spinal cord injury: applications for diaphragmatic pacing. *Muscle Nerve*. 2008 Dec;38(6):1546-52.
2. American Thoracic Society. Congenital central hypoventilation syndrome: genetic basis, diagnosis and management. Sep 2009. Accessed Jun 3, 2011. Available at URL address: <http://www.thoracic.org/statements/>
3. Avery Biomedical Devices, Inc. Breathing pacemakers. 2010. Accessed May 24, 2010. Available at URL address: <http://www.averylabs.com/>
4. Canadian Agency for Drugs and Technologies in Health (CADTH). Issues in Emerging Health Technologies 115. Laparoscopic diaphragm pacing for tetraplegia. Issue 115. Sep 2009. Accessed Jun 3, 2011. Available at URL address: http://www.cadth.ca/media/pdf/R0003_Laparoscopic_Diaphragm_Pacing_Tetraplegia_cetap_e.pdf
5. Chen ML, Tablizo MA, Kun S, Keens TG. Diaphragm pacers as a treatment for congenital central hypoventilation syndrome. *Expert Rev Med Devices*. 2005 Sep;2(5):577-85.
6. ECRI Institute. Intramuscular diaphragm stimulation for chronic respiratory failure. [Emerging Technology evidence report]. Plymouth Meeting (PA): ECRI Institute; 2010 Dec 10. Available at URL address: <http://www.ecri.org>.
7. Eleftheriades J, Quin J, Hogan J, Holcomb W, Letsou G. Long-term follow-up of pacing of the conditioned diaphragm in quadriplegia. *Pacing Clin Electrophysiol*. 2002 Jun;25(6):897-906.
8. Garrido-Garcia H, Mazaira Alvarez J, Martin Escribano P, Romero Ganuza J, La Banda F, Gambarrutta C, et al. Treatment of chronic ventilatory failure using a diaphragmatic pacemaker. *Spinal Cord*. 1998 May;36(5):310-4.
9. Hirschfeld S, Exner G, Luukkaala T, Baer GA. Mechanical ventilation or phrenic nerve stimulation for treatment of spinal cord injury-induced respiratory insufficiency. *Spinal Cord*. 2008 Nov;46(11):738-42.
10. National Institute for Health and Clinical Excellence (NICE). IPG307. Intramuscular diaphragm stimulation for ventilator dependent chronic respiratory failure due to neurological disease: guidance. Jul 22, 1009. Accessed Jun 3, 2011. Available at URL address: <http://guidance.nice.org.uk/IPG307>
11. Onders RP, Carlin AM, Elmo M, Sivashankaran S, Katirji B, Schilz R. Amyotrophic lateral sclerosis: the Midwestern surgical experience with the diaphragm pacing stimulation system shows that general anesthesia can be safely performed. *Am J Surg*. 2009 Mar;197(3):386-90.
12. Onders RP, Elmo MJ, Ignagni AR. Diaphragm pacing stimulation system for tetraplegia in individuals injured during childhood or adolescence. *J Spinal Cord Med*. 2007;30 Suppl 1:S25-9.
13. Onders RP, Elmo M, Khansarinia S, Bowman B, Yee J, Road J, Bass B, Dunkin B, Ingvarsson PE, Oddsdóttir M. Complete worldwide operative experience in laparoscopic diaphragm pacing: results and differences in spinal cord injured patients and amyotrophic lateral sclerosis patients. *Surg Endosc*. 2009 Jul;23(7):1433-40.

14. Onders RP, Khansarinia S, Weiser T, Chin C, Hungness E, Soper N, Dehoyos A, Cole T, Ducko C. Multicenter analysis of diaphragm pacing in tetraplegics with cardiac pacemakers: positive implications for ventilator weaning in intensive care units. *Surgery*. 2010 Oct;148(4):893-7; discussion 897-8.
15. Shaul D, Danielson P, McComb J, Keens T. Thoroscopic placement of phrenic nerve electrodes for diaphragmatic pacing in children. *J Pediatr Surg*. 2002 Jul;37(7):974-8.
16. Synapse Biomedical Inc. NeuRXDPS™ FAQs. 2008. Accessed May 24, 2010. Available at URL address: <http://www.synapsebiomedical.com/news/media/>
17. U.S. Food and Drug Administration (FDA). Part 882 neurological devices. Apr 1, 2010. Accessed Jun 3, 2011. Available at URL address: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?FR=882.5830>
18. U.S. Food and Drug Administration (FDA). PMA final decisions rendered for July 2000. P860026/S006. Accessed Jun 3, 2011. Available at URL address: <http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/ucm113948.htm>
19. U.S. Food and Drug Administration (FDA). Synapse-NeuRx DPS™ RA/4 Diaphragm Pacing Stimulation System - H070003. June 17, 2008. Accessed Jun 3, 2011. Available at URL address: <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cftopic/pma/pma.cfm?num=H070003>

Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare	07/15/2008	0391	Diaphragmatic/Phrenic Nerve Stimulation

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