SAMPLE COVER LETTER FROM PHYSICIAN TO MEDICARE MEDICAL DIRECTOR TO REQUEST COVERAGE FOR MEDICARE BENEFICIARIES

Provider letterhead

Date

Address of Medicare Contractor

Dear Dr. _____:

Re: Request for Reimbursement for use of the NeuRx® DPS System™ to Manage ALS-Related Hypoventilation in Appropriate Patients at our Facility

This letter is to advise you that [*Name of Institution*], (NPI 000000), will provide the NeuRx® Diaphragm Pacing (DPS) System™. to appropriate patients for the management of chronic hypoventilation associated with amyotrophic lateral sclerosis (ALS).

The NeuRx® DPS System™, ' manufactured by Synapse Biomedical, Inc., is approved by FDA as a Humanitarian Use Device (HUD) under a Humanitarian Device Exemption[1] for ALS patients with a stimulatable diaphragm (both right and left portions) demonstrated by voluntary contraction or phrenic nerve conduction studies, who are experiencing chronic hypoventilation (CH), but have not progressed to a Forced Vital Capacity (FVC) less than 45% predicted where CH is demonstrated either by FVC < 50% predicted, Maximal Inspiratory Pressure (MIP) < 60 cm H_2O, or Oxygen Saturation SaO2 ≥88% for at least five continuous minutes or PCO2 ≥ 45 mm Hg. The DPS System is approved for use in patients 21 years of age or older.

As you know, FDA approves a HUD when "the probable benefit to health from the use of the device outweighs the risk of injury or illness, taking into account the probable risks and benefits of currently available forms of treatment."[2]

Accordingly, I am submitting the attached information to support a request for reimbursement for services associated with the use of the device, including facility and professional fees related to the purchase, electrode implant and calibration of the device for treatment of appropriate Medicare beneficiaries with ALS at our facility.

I have enclosed a complete dossier for your review containing the required documentation including:

- Approval from the [*Name of Institutional Review Board*]
- Sample informed consent form (OPTIONAL, if required by your local IRB)
- [*Name of Institution*] protocol for obtaining informed consent (OPTIONAL, if required by your local IRB)

---

[1] HDE -- # H100006

[2] 21 CFR § 814.118(a)(3). FDA regulations also require the labeling of all HUD's to state that the effectiveness of the product for its approved indication has not been demonstrated. 21 CFR § 814.104(b)(4)(ii).

- Device description
- FDA HDE approval letter
- Bibliography of peer-reviewed literature
- Full Prescribing Information

Please let me know if I can provide additional information. I may be reached at [*000-000-0000*]. Thank you for your attention to this important matter.

Sincerely,

[*Physician Name*], MD
Medicare Provider Number 00000000

Enclosure
cc: [*Part A/Part B*] Medical Director

SAMPLE REQUEST TO COMMERCIAL HEALTH INSURER FOR COVERAGE AND REIMBURSEMENT (OTHER THAN MEDICARE)

Date:

Patient Name
Patient DOB
Patient ID#
Group #

Medical Director
Name of Insurance Plan
Street address
City, state, zip

Dear Doctor _____:

Re: Request for Coverage for the NeuRx® DPS System™ (device and procedure)

I am writing to request coverage for implanting the NeuRx® Diaphragm Pacing (DPS) System™ in [PATIENT NAME] for the management of severe chronic hypoventilation associated with amyotrophic lateral sclerosis (ALS).

In my professional opinion, this procedure is medically necessary and appropriate for the patient. Evidence recently published in the peer reviewed literature supports the use of diaphragmatic phrenic nerve stimulation in management of severe chronic hypoventilation associated with ALS.

I. CLINICAL SUMMARY

[INSERT BRIEF SUMMARY TO DESCRIBE (PATIENT'S NAME'S) MEDICAL CONDITION AND RATIONALE FOR PROCEDURE. APPEND YOUR CLINICAL NOTES AS AN ATTACHMENT TO THE LETTER.]

Amyotrophic lateral sclerosis (ALS)

As you know, ALS is a progressive neurodegenerative disease that affects nerve cells in the brain and spinal cord. A typical patient will eventually require respiratory support, usually from a ventilator. Complications associated with severe chronic hypoventilation are a major cause of death among persons with ALS.

The phrenic nerve stimulator is intended to be an alternative to intermittent or permanent use of a mechanical ventilator and the risks of complications associated with maintaining a

permanent tracheotomy stoma. Selection of a phrenic nerve stimulator implanted laparoscopically further reduces health risks by eliminating the need for open thoracotomy. Phrenic nerve stimulation provides relief from mechanical ventilation and may contribute to significant improvement in quality of life.

II. DEVICE

The NeuRx® DPS System™, ' manufactured by Synapse Biomedical, Inc., is approved by FDA as a Humanitarian Use Device (HUD) under a Humanitarian Device Exemption[1] for ALS patients with a stimulatable diaphragm (both right and left portions) demonstrated by voluntary contraction or phrenic nerve conduction studies, who are experiencing chronic hypoventilation (CH), but have not progressed to a Forced Vital Capacity (FVC) less than 45% predicted, where CH is demonstrated either by FVC < 50% predicted, Maximal Inspiratory Pressure (MIP) < 60 cm H_2O or Oxygen Saturation SaO2 ≥88% for at least five continuous minutes or PCO2 ≥ 45 mm Hg. The DPS System is approved for use in patients 21 years of age or older.

Approval was based on results of a multi-center prospective study of the NeuRx® Diaphragm Pacing (DPS) System™ that evaluated motor-point stimulation for conditioning the diaphragm of subjects with amyotrophic lateral sclerosis (ALS). The study found that the probable benefit to health from use of the device outweighed the risk of injury or illness from its use.[2,3,4]

The NeuRx® DPS RA/4 Respiratory Stimulation System is implanted through minimally invasive laparoscopic surgery. It provides electrical stimulation to muscles and nerves that run through the diaphragm. This eliminates any direct contact with the phrenic nerve, allows all circuitry and electronics to remain outside the body, and provides direct, selective activation to each hemidiaphragm. The NeuRx® DPS device uses four electrodes implanted in the muscle of the diaphragm to stimulate contraction electronically; allowing the user to inhale. The DPS is lightweight and battery powered, eliminating the need for an external power source.

---

[1] HDE -- # H100006

[2] FDA/HDE; SSPB, 2011.

[3] FDA regulations also require the labeling of all HUD's to state that the effectiveness of the product for its approved indication has not been demonstrated. 21 CFR § 814.104(b)(4)(ii).

[4] Onders RP, Elmo MJ, Khansarinia S, et al. Complete worldwide operative experience in laparoscopic diaphragm pacing: results and differences in spinal cord injured patients and amyotrophic lateral sclerosis patients. *Surg Endosc* 2008; Dec 6. Published online: DOI 10.1007/s00464-008-0223-3.

Treatment plan

The protocol for managing ALS patients with chronic hypoventilation at our facility has been approved by the Institutional Review Board (IRB) in accordance with FDA regulation of HUDs. The patient will be treated as part of a post-approval study commitment that FDA required of the device manufacturer (Synapse Biomedical, Inc.) through which long term follow up data on device use will be collected.

As part of the study, [PATIENT NAME] will be evaluated for chronic hypoventilation prior to device implantation. Patients will be followed every 3 months for an average of 3 years to track the occurrence and timing of major device-related adverse events, capnothorax, mechanical ventilation for 24 hours or longer post procedure, perioperative complications delaying initiation of therapy, severe discomfort, device malfunction, electrode dislodgement, wire infection, and any other device- or procedure-related serious AE. Each NeuRx® DPS System implanted will be tracked to the end patient in accordance with FDA regulation.

Clinical/scientific evidence

Federal regulations allow FDA to approve the sale of a humanitarian use device when:

> . . . The probable benefit to health from the use of the device outweighs the risk of injury or illness, taking into account the probable risks and benefits of currently available forms of treatment.[5]

Valid scientific evidence

Data submitted to the FDA from the NeuRx® DPS IDE study (# G040142) in support of the HDE application show that patients with chronic hypoventilation identified either by Forced Vital Capacity (FVC) < 50 percent of predicted, or Maximal Inspiratory Pressure (MIP)< 60 cm H_2O, or Oxygen Saturation $SaO_2 \geq 88$ percent for at least five continuous minutes, or $PCO_2 \geq 45$ mm Hg[6,7] benefited from the treatment. In the 82 patient pivotal study, treatment outcomes included:

- Improved survival from the time of diagnosis (by 16 months) and from the start of non-invasive ventilation (NIV) (by nine months) compared to standard of care NIV;

---

[5] 21 CFR § 814.118(a)(3).

[6] Clinical Indications for Noninvasive Positive Pressure Ventilation in Chronic Respiratory Failure Due to Restrictive Lung Disease, COPD, and Nocturnal Hypoventilation—A Consensus Conference Report. *Chest* 1999;116(2) 521-534.

[7] Miller, R.G., et al., Practice parameter: the care of the patient with amyotrophic lateral sclerosis (an evidence-based review): Report of the Quality Standards Subcommittee of the American Academy of Neurology: ALS Practice Parameters Task Force. *Neurology* 1999;52(7):1311-23.

- A 100 percent 30-day survival rate of patients with simultaneous PEG and DPS compared to 30-day mortality expectations of 2 – 25 percent with continued long term improvement in survival;
- A 16-month survival from implant for patients with no other respiratory options who were intolerant of or unable to use NIV;
- Sleep improvement after four months of DPS conditioning: an increased sleep efficiency (median 9 percent), with a reduction in arousal index driving a decrease of wake after sleep onset (median 69 minutes). This is clinically significant because drugs widely prescribed for the treatment of primary insomnia increase sleep efficiency by 6-7 percent and reduce wake after sleep onset by 15-20 minutes.

These were the conclusions of the analyses of the cohort of the multicenter study population that satisfied the "humanitarian use designation" (HUD) clinical selection criteria which correspond to the approved indications for use. These results were published by FDA in its Summary of Safety and Probable Benefit for the approval of NeuRx DPS in HDE H100006. [8] Investigators in the multicenter study also authored preliminary, subset, and substudy reports which were published in medical journals. Onders and colleagues reported on the safety of the implantation procedure and the benefits in delaying the need for ventilators and increasing survival[9, 10]. Gonzalez and colleagues reported on the benefits in sleep.[11]

With prolonged use of the system to condition diaphragm musculature, the need for tracheostomy and mechanical ventilation can be delayed, reducing the risk of adverse events associated with these procedures. Data on ALS-related hospitalizations show that 36 percent of patients admitted to the emergency department were treated for pneumonia and 54.6 percent of these admissions required either short-term hospital, skilled nursing, intermediate, or home health care post discharge.[12] Other published data report an association between hours on a ventilator and ventilator-acquired pneumonia (VAP), infections, atelectasis and barotraumas.[13]

---

[8] FDA/HDE; SSPB, 2011.

[9] Onders RP, Elmo M, Khansarinia S, et al. Complete worldwide operative experience in laparoscopic diaphragm pacing: Results and differences in spinal cord injured patients and amyotrophic lateral sclerosis patients. *Surg Endosc*. 2009a;23(7):1433-1440.

[10] Onders RP, Carlin AM, Elmo M, et al. Amyotrophic lateral sclerosis: The midwestern surgical experience with the diaphragm pacing stimulation system shows that general anesthesia can be safely performed. *Am J Surg.* 2009b;197(3):386-390.

[11] Gonzalez-Bermejo J, Morélot-Panzini C, Salachas F, et al. Diaphragm pacing improves sleep in patients with amyotrophic lateral sclerosis. *Amyotroph Lateral Scler*. 2011 Oct 24. [Epub ahead of print].

[12] Lechtzin N, Wiener CM, Clawson L, et al. Hospitalization in amyotrophic lateral sclerosis: causes, costs, and outcomes. *Neurology* 2001;56(6): 753-7.

[13] Rello J, Ollendorf DA, Oster G, et al. Epidemiology and outcomes of ventilator-associated pneumonia in a large US database. *Chest* 2002;122(6):2115-2121.

III. COMMERCIAL INSURERS COVERING PHRENIC NERVE STIMULATION FOR ALS

Medicare, Aetna, Cigna and Wellpoint already cover and pay for phrenic nerve stimulation in management of chronic hypoventilation associated with ALS.

- Medicare:[14] The implantation of a phrenic nerve stimulator is covered for selected patients with partial or complete respiratory insufficiency. ALS is not explicitly excluded from coverage, allowing contractor medical directors freedom to cover the implant for management of severe chronic hypoventilation in ALS when it is reasonable and necessary.

- Aetna[15] considers diaphragmatic/phrenic pacing (e.g., the NeuRx DPS® RA/4 Respiratory Stimulation System) medically necessary for individuals with amyotrophic lateral sclerosis.

- Cigna[16] covers the NeuRx DPS® Diaphragm Pacing System™ for individuals age 21 years or older with ALS when provided in accordance with HDE specifications.

- Wellpoint[17] considers the NeuRx DPS® Diaphragm Pacing System™ to be medically necessary as an alternative to invasive mechanical ventilation in individuals with motor neuron disease, for example amyotrophic lateral sclerosis (ALS) when ALL of the following criteria are met:

    - Diaphragm movement with stimulation is visible under fluoroscopy; **and**
    - Stimulation of the diaphragm directly results in sufficient muscle activity to accommodate independent breathing without the support of a ventilator; **and**
    - Individual has normal chest anatomy, a normal level of consciousness, and has the ability to participate in and complete the training and rehabilitation associated with the use of the device.

---

[14] CIM 65-13 §160.19 - Phrenic Nerve Stimulator (Rev. 1, 10-03-03).

[15] Aetna clinical policy bulletin 0677: Functional electrical stimulation and neuromuscular electrical stimulation. Last reviewed 03/29/2012. See http://www.aetna.com/cpb/medical/data/600_699/0677.html

[16] Cigna medical coverage policy 0391: Diaphragmatic/Phrenic Nerve Stimulation. Last reviewed 07/15/2012. See http://www.cigna.com/assets/docs/health-care-professionals/coverage_positions/mm_0391_coveragepositioncriteria_diaphragmatic_phrenic_nerve_stimulation.pdf

[17] Anthem Wellpoint medical policy MED.00100: Diaphragmatic/phrenic nerve stimulation. Last reviewed 02/16/2012. See http://www.anthem.com/medicalpolicies/policies/mp_pw_b099011.htm

IV. CONCLUSION

Both the evidence and my own practice experience have convinced me that phrenic nerve stimulation in management of ALS-related severe chronic hypoventilation is medically necessary and appropriate for this patient. **For these reasons, we request coverage and payment for the implant procedure and associated facility costs as well the cost of the NeuRx DPS® System™ itself for [PATIENT NAME.] [OPTIONAL: The NeuRx DPS® System™ costs $ _____.]**

Attached is supplementary material including our institution's IRB approval, IRB approved informed consent form, the FDA HDE approval letter, coding information, relevant patient medical records, and a bibliography of peer-reviewed literature on phrenic nerve stimulation and diaphragm pacing. Full prescribing information is attached.

I appreciate your careful and expedited medical review and approval of this request. If you have any questions about this proposed treatment, please contact me at (XXX) XXX-XXXX. Please send your written decision to me at the address below.

Sincerely,

Attachments

V. ADDITIONAL REFERENCES FROM THE PEER REVIEWED LITERATURE

Gonzalez-Bermejo J, Morélot-Panzini C, Salachas F, et al. Diaphragm pacing improves sleep in patients with amyotrophic lateral sclerosis. *Amyotroph Lateral Scler*. 2011 Oct 24. [Epub ahead of print].

Miller RG, Jackson CE, Kasarskis EJ, et al. Practice parameter update: The care of the patient with amyotrophic lateral sclerosis: Drug, nutritional, and respiratory therapies (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology(AAN). *Neurology*. 2009; 73:1218-1226.

Onders RP, Elmo MJ, Khansarinia S, et al. Complete worldwide operative experience in laparoscopic diaphragm pacing: results and differences in spinal cord injured patients and amyotrophic lateral sclerosis patients. *Surg Endosc* 2008; Dec 6. Published online: DOI 10.1007/s00464-008-0223-3.

Onders RP et al, Study Results of Diaphragm Pacing in Extremely Low Forced Vital Capacity Patients with Amyotrophic Lateral Sclerosis/Motor Neuron Disease: Is there a Role at End Stage ALS? *ALS/MDA Sessions* 2010.