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Via Electronic Submission

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Steve Phurrough, M.D., M.P.A.  
Director Coverage and Analysis Group  
Centers for Medicare and Medicaid Services  
7500 Security Boulevard  
Baltimore, MD 21244

**RE: Formal Request for Reconsideration  
Vagus Nerve Stimulation (VNS) Therapy System for the Treatment of Seizures and  
Depression  
National Coverage Decision (NCD) 160.18, Coverage Issue Manual 60-22  
Benefit Category: Durable Medical Equipment (DME)**

Dear Dr. Phurrough:

On behalf of Cyberonics, Inc., thank you for your acceptance of this Formal Request for Reconsideration of the existing National Coverage Decision 160.18. The benefit category under consideration is Durable Medical Equipment.

As you are aware, the United States Food and Drug Administration (FDA) approved the VNS Therapy System for the indication of refractory epilepsy on July 16, 1997. CMS issued its National Coverage Decision through Transmittal 144. CMS amended its Coverage Manual (§60-22) as follows:

"Clinical evidence has shown that vagus nerve stimulation is safe and effective treatment for patients with medically refractory partial onset seizures, for whom surgery is not recommended or for whom surgery has failed. Vagus nerve stimulation is not covered for patients with other types of seizure disorders which are medically refractory and for whom surgery is not recommended or for whom surgery has failed."

The FDA expanded the indications for use of the VNS Therapy System on July 15, 2005 to include patients with treatment resistant depression (TRD). The specific indication for use in TRD is as follows:

"The VNS Therapy System is indicated for the adjunctive long-term treatment of chronic or recurrent depression for patients over the age of 18 who are experiencing a major depressive episode and have not had an adequate response to four or more adequate antidepressant treatments."

The safety and effectiveness of the VNS Therapy System for patients with TRD was established during a 7-year clinical development program preceding the FDA approval of the TRD indication. The FDA summary of safety and effectiveness for the TRD indication stated:

"In conclusion, the Center for Devices and Radiological Health (CDRH) believes the PMA applicant has provided reasonable assurance of safety and efficacy based on valid scientific evidence as required by statute and regulation for the approval of a Class III medical device.

CDRH has come to this conclusion because the sponsor has provided data that were systematically collected and analyzed which showed significant improvement from baseline over one and two years for a definable subset of the target population, and comparative data against a reasonably matched control which also sustained improvement over time."

To date, physicians have used VNS Therapy to treat in excess of 40,000 patients with refractory epilepsy, resulting in more than 100,000 patient-years of experience. This experience has confirmed the clinical effectiveness, safety, and cost-effectiveness of VNS Therapy for patients with refractory epilepsy. Since the FDA approval of the TRD indication, physicians have used the VNS Therapy System to treat more than 1,500 patients with TRD. The early post-marketing safety and effectiveness experience for VNS Therapy in patients with TRD has been similarly favorable to the experience in patients with refractory epilepsy. While some local carriers have not yet provided coverage for the VNS Therapy System for the TRD indication, these carriers have not had access to, nor reviewed in its entirety, all scientific publications, poster presentations and reports that have been included within this Application.

Cyberonics is proposing that CMS amend their current coverage policy for the VNS Therapy System to include a subset of the patients who meet the FDA-labeled indication for use in TRD. This subset, which is referred to in the application as patients with TRDEH, is comprised of those who have had or refused electroconvulsive therapy (ECT) for the treatment of depression or who have been hospitalized for the treatment of depression. Cyberonics is confident that your careful analysis of the enclosed application will result in the conclusion that the VNS Therapy System is medically necessary for patients with TRDEH because the prognosis for treatment-resistant depressed patients treated with standard antidepressant treatments is typically poor. There is no evidence that any other FDA-approved antidepressant treatment reliably provides *durable* safety and effectiveness for the patient who is resistant to multiple standard antidepressant treatments. Unproven and ineffective treatment options for this refractory population continue to result in inferior outcomes for patients and for Medicare. Additionally, there is good evidence that the group of patients who meet the criteria for TRDEH consumes a vastly disproportionate and excessive amount of health care resources and dollars. Owing to disability, many of these TRDEH patients will become Medicare beneficiaries prematurely. Cyberonics is also confident that your careful analysis of the enclosed application will result in the conclusion that the VNS Therapy System is reasonable for patients with TRDEH because the VNS Therapy System is the only treatment approved by the FDA specifically for TRD. In the premarketing clinical trials of the VNS Therapy System for the TRD indication, adjunctive VNS Therapy produced statistically and clinically significantly superior outcomes vs. treatment-as-usual using standard antidepressant treatments.

Thank you again for your review and acceptance of this Formal Request for Reconsideration.

Sincerely,



RICHARD L. RUDOLPH, M.D.  
Vice President, Clinical & Medical Affairs  
and Chief Medical Officer  
Cyberonics, Inc.