1 INTENDED USE / INDICATIONS

Epilepsy (US)—The VNS Therapy System is indicated for use as an adjunctive therapy in reducing the frequency of seizures in adults and children over 12 years of age with partial onset seizures refractory to antiepileptic medications.

2 CONTRAINDICATIONS

Vagotomy—The VNS Therapy System cannot be used in patients after a bilateral or left cervical vagotomy.

Diathermy—Do not use short-wave diathermy, microwave diathermy, or therapeutic ultrasound therapy on a patient who has the VNS Therapy System. Diagnostic ultrasound is not included in this contraindication.

3. WARNINGS — GENERAL

Physicians should inform patients about all potential risks and adverse events discussed in the physician’s manuals. This document is not intended to serve as a substitute for the complete physician’s manuals.

The safety and efficacy of the VNS Therapy System have not been established for uses outside the “Intended Use/Indications” section of the physician’s manuals.

The safety and effectiveness of the VNS Therapy System in patients with predisposed dysfunction of cardiac conduction systems (re-entry pathway) have not been established. Post-implant electrocardiography is recommended if clinically indicated.

Postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. It is important to follow recommended implantation procedures and intraoperative product testing described in the Implantation Procedure part of the physician’s manuals. During the intraoperative System Implantation Procedure, Diagnostic and Patient Assessment System (DAPS) optimal parameters or bradycardia alert mode have occurred. If asystole, severe bradycardia (heart rate < 40 bpm), or a clinically significant change in heart rate is encountered during a System Diagnostics (Lead Test) or during initiation of stimulation, physicians should be prepared to follow guidelines consistent with Advanced Cardiac Life Support (ACLS).

Difficult swallowing (dysphagia) may occur with active stimulation, and aspiration may result from the oral or pharyngeal swarming difficulties. Patients with pre-existing swallowing difficulties are at greater risk for aspiration.

Dyspnea (shortness of breath) may occur with active VNS Therapy. Any patient with underlying pulmonary disease, for example, chronic obstructive pulmonary disease or asthma might be at increased risk for dyspnea.

Patients with obstructive sleep apnea (OSA) may have an increase in apneic events during stimulation. Lowering stimulus frequency or prolonging “OFF” time may prevent exacerbation of OSA. Vagus nerve stimulation can cause new onset sleep apnea in patients who have not previously been diagnosed with this disorder.

Device malfunction could cause painful stimulation or direct current stimulation. Either event could lead to severe damage to the patient if the stimulus is not immediately turned off. If the patient suspects a malfunction, and then to contact their physician immediately for further evaluation.

Patients with the VNS Therapy System, or any part of the VNS Therapy System, implanted should have a fragment of the system removed if a subsequent procedure (e.g., coronary bypass surgery, abdominal surgery, orthopedic surgery) will require the removal of the VNS Therapy System if a scan using a transmit RF body coil is needed.

Excessive stimulation at an excess duty cycle (that is, one that occurs when “ON” time is greater than “OFF” time) and high frequency stimulation (i.e., stimulation at ≥ 50 Hz) has resulted in degenerative nerve damage in laboratory animal studies.

Patients who manipulate the pulse generator and lead through the skin (Twiddler’s Syndrome) of disconnection or disconnect the lead from the pulse generator and/or possibly damage cause the vagus nerve.

Cardiac arrhythmia (Model 106 only)—The AutoStim Mode feature should not be used in patients with clinicardiology devices. These devices interfere with normal intrinsic heart rate responses (e.g., pacemaker dependency, implantable defibrillators, beta adrenergic blocker medications). Patients also should not have a history of chronotropic incompetence (commonly seen in patients with sustained bradycardia (heart rate < 50 bpm)).

Pre-surgical Surface Assessment (Model 106 only)—For anticipated use of the AutoStim feature, it is important to perform a pre-surgical surface assessment prior to the Implantation Procedure to determine a location for the pulse generator to reside in which it can accurately detect heart beat.

4 WARNINGS — EPILEPSY

The VNS Therapy System should only be prescribed and monitored by physicians who have specific training and expertise in the management of seizures and the use of this device. It should only be implanted in patients who have been rationally treated and consult with a physician before engaging in unsupervised activities, such as driving, swimming, and bathing, and in strenuous sports that could harm them or others.

Sudden unexpected death in epilepsy (SUDEP). Through August 1996, 10 sudden and unexpected deaths have been reported among the 1,000 patients implanted and treated with the VNS Therapy device. During this period, these patients had accumulated 2,017 patient-years of exposure. Some of these deaths could represent seizure-related deaths in which the seizure was not observed, at night, for example. This number represents an incidence of 5.0 definite, probable, and possible SUDEP deaths per 1,000 patient-years of exposure. Surviving patients and Holter monitors are recommended by the VNS Therapy System’s Implantation Procedure for those patients who are difficult to treat and may require that the device be explanted. The patient should be given additional drug therapy preoperatively. The surgeon should ensure that all instruments are sterile prior to the procedure.

The VNS Therapy System may affect the operation of other implanted devices, such as cardiac pacemakers and implanted defibrillators. Possible effects include sensing problems and inappropriate shocks. For patients with non-currrent implantable cardiac pacemakers or defibrillators, the VNS Therapy System is not recommended for use.

Reversal of lead polarity has been associated with an increased chance of bradycardia in animal studies. It is important that the electrodes are attached to the left vagus nerve in the correct orientation. It is also important to make sure that leads with dual connector pins are correctly inserted (white marker band to + connection) into the pulse generator’s lead receptacles.

The patient can use a neck brace for the first week to help ensure proper lead stabilization.

Do not program the VNS Therapy System to an “ON” or periodic stimulation treatment for at least 14 days after the initial or replacement implantation.

For Models 100, 101, 102 and 102R do not use frequencies of 5 Hz or below for long-term stimulation.

Resetting the pulse generator disables or turns the device OFF (output current = 0 mA). For Model 100, 101, 102 and 102R, resetting the pulse generator will result in device history loss.

5. ADVERSE EVENTS — EPILEPSY

Adverse events reported during clinical studies as statistically significant are listed below in order of seriousness.