

Vagus Nerve Stimulation

Brief Summary of Safety Information for the VNS Therapy™ System
(Depression Indication)
(July 2005)

1. Intended Use / Indications: Depression (USA)

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

2. Contraindications

The VNS Therapy System cannot be used in patients after a bilateral or left cervical vagotomy. Do not use short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy on patients implanted with a VNS Therapy System. Diagnostic ultrasound is not included in this contraindication.

3. Warnings

Physicians should inform patients about all potential risks and adverse events discussed in the Physician's Manuals (Depression). This document is not intended to serve as a substitute for the complete Physician's Manuals (Depression).

This device is a permanent implant. It is only to be used in patients with severe depression who are unresponsive to standard psychiatric management. It should only be prescribed and monitored by physicians who have specific training and expertise in the management of treatment-resistant depression and use of this device. It should only be implanted by physicians who are trained in surgery of the carotid sheath and have received specific training in the implantation of this device.

Physicians should warn patients that VNS Therapy has not been determined to be a cure for depression.

The safety and efficacy of the VNS Therapy System have not been established for uses not covered in the "Intended Use/Indications" section of the Physician's Manuals (Depression and Epilepsy).

Patients being treated with adjunctive VNS Therapy should be observed closely for clinical worsening and suicidality, especially at the time of VNS Therapy stimulation parameter changes or drug or drug dose changes.

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.

Postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. Post-implant electrocardiograms and Holter monitoring are recommended if clinically indicated.

It is important to follow recommended implantation procedures and intraoperative product testing described in the Physician's Manuals (Epilepsy and Depression). During the intraoperative System Diagnostics (Lead Test), infrequent incidents of bradycardia and/or asystole have occurred. If asystole, severe bradycardia (heart rate <40 bpm), or a clinically significant change in heart rate is encountered during a System Diagnostics or during initiation of stimulation, physicians should be prepared to follow guidelines consistent with Advanced Cardiac Life Support (ACLS).

Difficulty swallowing (dysphagia) may occur with active stimulation, and aspiration may result from the increased swallowing difficulties. Patients with pre-existing swallowing difficulties are at greater risk for aspiration.

Shortness of breath (dyspnea) may occur with active VNS Therapy. Any patient with underlying pulmonary disease or insufficiency such as chronic obstructive pulmonary disease or asthma may 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 may also 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 cause nerve damage. Patients should be instructed to use the Magnet to stop stimulation if they suspect 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 not have full body MRI.

Use of the Magnet to activate stimulation is not recommended for patients with depression.

Excessive stimulation at an excess duty cycle has resulted in degenerative nerve damage in laboratory animals.

Patients who manipulate the Pulse Generator and Lead through the skin may damage or disconnect the Lead from the Pulse Generator and/or possibly cause damage to the vagus nerve.

4. Precautions

Physicians should inform patients about all potential risks and adverse events discussed in the Physician's Manuals (Depression).

Prescribing physicians should be experienced in the diagnosis and treatment of epilepsy or depression and should be familiar with the programming and use of the VNS Therapy System.

Physicians who implant the VNS Therapy System should be experienced performing surgery in the carotid sheath; physicians should be familiar with vagus nerve anatomy, particularly the cardiac branches; and they should be trained in the surgical technique relating to implantation of the VNS Therapy System.

The safety and effectiveness of the VNS Therapy System have not been established for use during pregnancy. VNS should be used during pregnancy only if clearly needed.

The VNS Therapy System is indicated for use only in stimulating the left vagus nerve in the neck area inside the carotid sheath. The VNS Therapy System is indicated for use only in stimulating the left vagus nerve below where the superior and inferior cervical cardiac branches separate from the vagus nerve.

It is important to follow infection control procedures. Infections related to any implanted device are difficult to treat and may require that the device be explanted. The patient should be given antibiotics 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 device responses. If the patient requires concurrent implantable pacemaker, defibrillatory therapy or other types of stimulators, careful programming of each system may be necessary to optimize the patient's benefit from each device.

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 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.

Do not use frequencies of 5 Hz or below for long-term stimulation.

Resetting the Pulse Generator turns the device OFF (output current = 0.0 mA), and all device history information is lost.

Patients who smoke may have an increased risk of laryngeal irritation.

5. Environmental And Medical Therapy Hazards

Patients should exercise reasonable caution in avoiding devices that generate a strong electric or magnetic field. If a Pulse Generator ceases operation while in the presence of electromagnetic interference (EMI), moving away from the source may allow it to return to its normal mode of operation.

VNS Therapy System operation should always be checked by performing device diagnostics after any of the procedures mentioned in the Physician's Manuals (Epilepsy and Depression).

For clear imaging, patients may need to be specially positioned for mammography procedures, because of the location of the Pulse Generator in the chest.

Therapeutic radiation may damage the Pulse Generator's circuitry, although no testing has been done to date and no definite information on radiation effects is available. Sources of such radiation include therapeutic radiation, cobalt machines, and linear accelerators. The radiation effect is cumulative, with the total dosage determining the extent of damage. The effects of exposure to such radiation can range from a temporary disturbance to permanent damage, and may not be detectable immediately. External defibrillation may damage the Pulse Generator.

Use of electrosurgery (electrocautery or radio frequency (RF) ablation devices) may damage the Pulse Generator.

Magnetic resonance imaging (MRI) should not be performed with a magnetic resonance body coil in the transmit mode. The heat induced in the Lead by an MRI body scan can cause injury. If an MRI should be done, use only a transmit-and-receive type of head coil. MRI compatibility was demonstrated using a 1.5T General Electric Sigma Imager with a Model 100 only. When other MRI systems are used, adverse events may occur because of different magnetic field distributions. Consider other imaging modalities when appropriate.

Procedures in which the radiofrequency (RF) is transmitted by the body coil should not be done on a patient who has the VNS Therapy System. Thus, protocols must not be used which utilize local coils that are RF receive-only, with RF-transmit performed by the body coil. Note that some RF head coils are receive only, and that most other local coils, such as knee and spinal coils, are also RF receive only. These coils must not be used in patients with the VNS Therapy System.

Extracorporeal shockwave lithotripsy may damage the Pulse Generator. If therapeutic ultrasound therapy is required, avoid positioning the area of the body where the Pulse Generator is implanted in the water bath or in any other position that would expose it to ultrasound therapy. If that positioning cannot be avoided, program the Pulse Generator output to 0 mA for the treatment, and then after therapy, reprogram the Pulse Generator to the original parameters.

If the patient receives medical treatment for which electric current is passed through the body (such as from a TENS unit), either the Pulse Generator should be set to 0 mA or function of the Pulse Generator should be monitored during initial stages of treatment.

Routine therapeutic ultrasound could damage the Pulse Generator and may be inadvertently concentrated by the device, causing harm to the patient. For information related to home occupational environments, cellular phones, other environmental hazards, other devices, and ECG monitors, please refer to the Physician's Manuals (Epilepsy and Depression) for complete information.

6. Adverse Events

Implant-related adverse events reported during the pivotal study in = 5% of patients are listed in order of decreasing occurrence: incision pain, voice alteration, incision site reaction, device site pain, device site reaction, pharyngitis, dysphagia, hypesthesia, dyspnea, nausea, headache, neck pain, pain, paresthesia, and cough increased.

Stimulation-related adverse events reported during the acute sham-controlled study by > 5% of VNS Therapy-treated patients are listed in order of decreasing occurrence: voice alteration, cough increased, dyspnea, neck pain, dysphagia, laryngismus, paresthesia, pharyngitis, nausea, and incision pain.

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1 The information contained in this Brief Summary for Physicians represents partial excerpts of important prescribing information taken from the Physician's Manuals (Epilepsy and Depression). (Copies of VNS Therapy Physician's and Patient's Manuals are posted at www.VNSTherapy.com/manuals.) The information is not intended to serve as a substitute for a complete and thorough understanding of the material presented in all of the Physician's Manuals for the VNS Therapy System and its component parts nor does this information represent full disclosure of all pertinent information concerning the use of this product, potential safety complications, or efficacy outcomes.

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