Looking forward

Your guide to VNS Therapy™

What to expect when moving forward
with LivaNova's VNS Therapy™ System.

LivaNova Epilepsy | VNS Therapy™

Congratulations on taking the next step to reimagine seizure control

VNS Therapy™ has been proven to not only help reduce the number of seizures—it may also shorten the length and severity of seizures that do occur and improve post-seizure recovery. Plus, VNS Therapy has been shown to improve over time to help control seizures for years to come.

VNS Therapy™ delivers stimulation in 3 ways

Normal Mode

Helps prevent seizures.

Stimulation is delivered in regular intervals all day, every day to help prevent seizures.

AutoStim Mode*

Responds to rapid increases in heart rate.

An extra stimulation is automatically delivered at the sign of a rapid increase in heart rate, which may be associated with seizures.

Magnet Mode

Delivers on-demand treatment.

Stimulation is manually delivered by swiping the included VNS Therapy Magnet over the generator to help stop or shorten a seizure once it starts.

*Only available in models 106 and 1000.

Visit VNSTherapy.com for more information.

Customized treatment with VNS Therapy™

The latest technology behind VNS Therapy™ includes features that offer treatment customization and easier management.

Scheduled Programming†

Allows the doctor to program the device to automatically increase therapy settings at intervals he or she chooses in advance until the targeted dose is reached. This option can save time and reduce the need for follow-up programming appointments.

Day/Night Programming†

Is an optional feature that allows the doctor to customize VNS Therapy based on lifestyle preferences or side effect management. The doctor can program the device to different settings for any two periods of time during a 24-hour period.

†Only available in Model 1000.

See pages 16 through 19 for Important Safety Information.

Preparing and fine-tuning

In the coming weeks and months, the doctor may want to schedule appointments to help prepare for the procedure.

After the VNS Therapy™ device has been implanted, the doctor will arrange for a series of follow-up appointments. Everyone is unique. These appointments allow the doctor to do a post-procedure assessment and fine tune dosing for the best possible results.

It's important to keep all appointments with the healthcare team.

Use this chart to keep track of appointments.‡

TYPE OF APPOINTMENT	DATE	TIME
Pre-surgery consultation		
Surgery		
Post-surgery follow-up (1-2 weeks after surgery)		
1st Dosing follow-up		
2nd Dosing follow-up		
3rd Dosing follow-up		
4th Dosing follow-up		
5th Dosing follow-up		
6th Dosing follow-up		
7th Dosing follow-up		

‡Dosing appointments required may vary.

Remember to bring the VNS Therapy™ Magnet to follow-up appointments with the neurologist.

Visit VNSTherapy.com for more information.

Create a caregiver network and keep everyone up to date

It's a good idea to keep family and friends informed about the decision to start VNS Therapy™.

Consider extending this network by educating teachers, school aids, and trusted work colleagues about what to do in case of a breakthrough seizure.

Let them know what to look for

Take a few minutes to reach out to everyone in your caregiver network and describe the signs and symptoms of a seizure. Remember, seizures are as unique as the individuals who have them. Be specific. A good description can help people in the caregiver network identify them, too.

Help them know what to do

Talk to people in your caregiver network about the VNS Therapy Magnet and show them how it works. Provide them with the contact information for the Clinical Nurse Education Specialist (CNES) or Care Coordinator. The people you share this information with may include school nurses, teachers, friends, and colleagues.

See pages 16 through 19 for Important Safety Information.

The VNS Therapy™ Magnet

The VNS Therapy™ Magnet allows patients and caregivers to manually deliver an extra stimulation, which may stop a seizure once it starts, help shorten the duration of a seizure, and improve recovery time after seizures.

The benefit of the magnet

The VNS Therapy device works to provide seizure control by automatically delivering stimulation at regular intervals throughout the day. The magnet is an optional benefit that may provide additional seizure control should a breakthrough seizure occur. It can also be used to temporarily suspend therapy.

Reasons to use the magnet

Use the VNS Therapy magnet when it's necessary to:

1. Start stimulation when a seizure is coming on or any time during a seizure.
2. Stop stimulation if it is painful or for activities like giving a speech or singing.
3. Test that the device is operating properly.

Visit VNSTherapy.com for more information.

How to use Magnet Mode

It's important for patients and caregivers to know how to use the VNS Therapy™ Magnet.

Acting quickly and effectively in the event of a seizure can make a difference. Fortunately, the VNS Therapy Magnet can be used to easily deliver an extra stimulation.

1. Remain calm

Having a level head will help you react appropriately and better manage the situation.

2. Locate the VNS Therapy Magnet

VNS Therapy patients often wear their magnet around their wrist or on their belt so they know where to find it. If it can be done safely, caregivers can unclip the magnet from their wrist or belt. That will make it easier to use when assisting someone having a seizure.

3. Use the VNS Therapy Magnet

The generator is typically located on the left side of the chest, close to the heart. Pass the magnet over the device for less than two seconds. This will trigger the implanted device to deliver an extra stimulation.

4. If necessary, use the magnet again

The magnet can be used more than once during a seizure. It's safe and will not damage the device, so don't be afraid to provide an extra stimulation.

5. Follow seizure protocol

If the seizure does not subside, contact the neurologist and follow their instructions.

See pages 16 through 19 for Important Safety Information.

The procedure

Now that the decision has been made to treat Drug Resistant Epilepsy (DRE) with VNS Therapy™, it's important to have a clear understanding of what the journey ahead looks like.

Here's a glimpse into who the procedure is for, and what can be expected.

Who can get VNS Therapy™?

VNS Therapy is a treatment designed for people with DRE 4 years of age and older with partial onset seizures that are refractory to antiepileptic medications.

What is the procedure like?

With VNS Therapy a small device (generator) is implanted in the chest and a thin wire, known as the lead, connects the device to the vagus nerve in the neck. This outpatient procedure usually takes 1 to 2 hours. It involves two small incisions and is typically performed under general anesthesia.

What happens after the procedure?

Most people go home the same day or the day following the procedure. The doctor will schedule a series of follow-up appointments to program the device for the best stimulation settings.

Visit VNSTherapy.com for more information.

Having an MRI

With the latest VNS Therapy™ technology, MRI is now more accessible than ever—provided specific guidelines are followed.

These steps should be followed before, during, and after an MRI with VNS Therapy:

1. **Before scheduling the MRI appointment**
   - Contact the neurologist to discuss the upcoming MRI
2. **Schedule the MRI appointment**
   - When making an appointment for an MRI, inform the MRI center about the implanted vagus nerve stimulator
   - Provide the model number of the implanted VNS Therapy device, as well as the name and contact information of the appropriate neurologist. This information can be found on the Patient MRI Form which will be provided by the neurologist
3. **Before the MRI**
   - The neurologist will temporarily turn the VNS Therapy device OFF and provide a copy of the Patient MRI Form to take to the MRI center
4. **Attend the MRI appointment**
   - Remember to bring the Patient MRI Form
   - Inform the radiologist and MRI technicians of the implanted VNS Therapy device and associated seizures
   - Do not bring the patient magnet into the MRI scanner room
   - Immediately alert the technician to any discomfort experienced during the MRI
5. **After the MRI**
   - Make an appointment with the neurologist to turn the VNS Therapy device back ON

See pages 16 through 19 for Important Safety Information.

Frequently asked questions

The Procedure

Are there risks linked with the surgery?

The most common side effect of the VNS Therapy™ implant procedure is infection. As with most surgical procedures, there are some standard risks. The neurologist and surgeon will discuss these risks.

Will the procedure be covered by insurance?

Many insurance companies cover the cost of VNS Therapy, including Medicare and Medicaid. Call **1-888-867-7846** to have one of our Care Coordinators help verify your benefits.

Will the implant device be visible to others?

The generator is small, not more than 2 inches (5 cm) in diameter depending on the model. For people with a small or thin frame, the shape of the device may be visible below the left collarbone. The lead is tunneled under the muscle and will not be visible. If this is a concern, we recommend discussing with the doctor.

Will the scars be noticeable?

Each person has different healing and scarring results. Some scarring should be expected from the procedure. If scarring is a special concern, we recommend discussing this with the surgeon.

Are there any special concerns when traveling?

Just as someone might carry an identification card if they had a pacemaker, the same is true of the VNS Therapy device. While a metal detector or screening booth will not cause harm or damage the VNS Therapy device, it may be advisable to request a wand examination to avoid setting off any alarms. A pat-down check may also be requested instead of walking through metal detectors.

Visit VNSTherapy.com for more information.

The Magnet

How often can the magnet be used?

Use the magnet for extra stimulation as often as necessary, but no more than 8 hours (continuous stimulation). Constant or frequent use of the magnet will use up the battery in the generator and could hurt the nerve. If the magnet is used often, the device settings may need to be adjusted. This is something to discuss with the doctor.

Depending on the settings, using the magnet will provide an additional 7 to 60 seconds of stimulation each time it is used. Using the magnet again during the same period will not make the stimulation stronger but will restart the magnet stimulation. Wait until the stimulation ends before trying it again.

Can all seizures be stopped with the magnet?

Results from magnet stimulation differ for each person.

Is it possible to stop all stimulation using the magnet?

Yes. To stop stimulation, hold the magnet over the generator and keep it there (some people use tape). If you have unusual or painful stimulation, contact the doctor immediately.

Will the magnet affect the normal treatment schedule?

The magnet overrides your normal treatment schedule, whether or not the device is ON at the time. Once the magnet-activated stimulation ends, the device will return to the treatment schedule set by your doctor.

See pages 16 through 19 for Important Safety Information.

Frequently asked questions

The Magnet (cont'd)

Can electronic devices affect the magnet, or will the magnet damage other electronic devices?

The magnet should be kept at least 10 inches (25 cm) away from credit cards, televisions, computers, microwave ovens, and other magnets.

Can I use any magnet with the VNS Therapy™ device?

No, the VNS Therapy™ Magnet is the only magnet that should be used with the VNS Therapy System.

How long will the magnet last?

With normal use, the VNS Therapy Magnet should last about 3 years.

Will dropping the magnet affect its strength?

The magnet's strength should not be affected if it is dropped. This is a common problem with low-power magnets.

Where do you get a new magnet?

Patients should receive two magnets when the device is implanted. Please contact the doctor for additional magnets.

Visit VNSTherapy.com for more information.

Having an MRI

Can a person have an MRI with VNS Therapy™?

MRI can safely be performed with the VNS Therapy™ System provided specific guidelines are followed. Speak to the doctor about which areas of the body can be safely scanned. MRI scan requirements are different depending on the VNS Therapy generator model and implant location.

What parts of the body can get scanned during an MRI?

Depending on the model and placement of the implanted VNS Therapy System, MRI of the head, neck, pelvis, lower spine, legs, arms, and other extremities can be safely performed with VNS Therapy System. Consult with the doctor who manages the VNS Therapy System prior to receiving an MRI. The doctor will determine which areas of your body can be safely scanned.

Is a special MRI center required to get an MRI?

No. Anyone with the VNS Therapy System may have an MRI safely performed at any MRI center that has a 1.5T or 3T MRI machine, provided that specific MRI guidelines are followed.

Should the magnet be within reach during an MRI?

No. Do not bring the magnet in the room with the MRI scanner.

What if a seizure occurs during an MRI?

If a seizure occurs during an MRI, medical personnel will follow protocol and stop the MRI immediately to apply standard first aid measures. Because of this possibility it is very important to let the technicians and nurses know about the seizure disorder prior to the MRI.

See pages 16 through 19 for Important Safety Information.

Questions for your neurologist or surgeon

Visit VNSTherapy.com for more information.

Additional notes

See pages 16 through 19 for Important Safety Information.

Safety information for VNS Therapy™

1. INDICATIONS

The VNS Therapy System is indicated for use as an adjunctive therapy in reducing the frequency of seizures in patients 4 years of age and older with partial onset seizures that are refractory to antiepileptic medications.

2. CONTRAINDICATIONS

Vagotomy — The VNS Therapy System should not be used (is contraindicated) in people who have had the left vagus nerve cut to treat another disorder (a left vagotomy).

Diathermy — Inform anyone treating you that you CANNOT have any short-wave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (hereafter referred to as "diathermy") anywhere on your body because you have an implanted VNS Therapy System (sometimes referred to as a "Vagus Nerve Stimulator" or "Vagus Nerve Stimulation"). Injury or damage can occur during diathermy treatment whether your VNS Therapy System is turned "ON" or "OFF." Diagnostic ultrasound is not included in this contraindication.

3. WARNINGS

Avoid excessive vagus nerve stimulation — Excessive stimulation of the vagus nerve can be produced by frequent magnet activation or more than 4 hours of continuous stimulation due to repeated magnet activations.

Unapproved uses — The safety and efficacy of the VNS Therapy System have not been established for uses outside its approved indications for use. The safety and efficacy of VNS Therapy have not been shown for people with these conditions: history of previous therapeutic brain surgery or brain injury, dysautonomias, lung diseases or disorders, including shortness of breath and asthma, ulcers (gastric, duodenal, or other), fainting (vasovagal syncope); irregular heartbeats (heart arrhythmias) or other heart abnormalities; other concurrent forms of brain stimulation; pre-existing hoarseness; under 4 years of age; progressive neurological diseases other than epilepsy.

Swallowing difficulties — Difficulty swallowing may occur with active stimulation, and aspiration may result from the increased swallowing difficulties. Use of the magnet to temporarily stop stimulation while eating may mitigate the risk of aspiration.

Shortness of breath — Shortness of breath may occur with active VNS Therapy, especially if you have chronic obstructive pulmonary disease or asthma.

Obstructive sleep apnea — Use of the VNS Therapy device can cause or worsen pre-existing obstructive sleep apnea (episodes where breathing stops for short periods of time while sleeping). You should see your physician if you show any signs or symptoms of obstructive sleep apnea or worsening obstructive sleep apnea.

Device malfunction — Device malfunction could cause painful stimulation or direct current stimulation. Either event could cause nerve damage and other associated problems.

Device removal — Removal of the VNS Therapy System requires an additional surgical procedure. When a device is removed, the surgeon may leave part of the lead behind. This may pose certain risks.

Device manipulation — Do not manipulate the generator and lead through the skin, as this may damage or disconnect the lead from the generator and/or possibly cause damage to the vagus nerve.

Device trauma — Blunt trauma to the neck and/or any area of the body beneath which the lead is implanted could possibly cause damage to the lead.

Not a cure — The VNS Therapy System does not stop all seizures. Continue to avoid activities that can be hazardous to you and others, such as driving and swimming alone.

Before having any MRI performed — Call your doctor, so your VNS Therapy System can be discussed with the MRI personnel. In many cases, an MRI can be performed safely under certain conditions. However, for a few other cases, surgery may be required to remove the VNS Therapy System prior to an MRI. Before undergoing an MRI scan with your VNS Therapy System, the VNS system diagnostic information will be collected and the current turned off. The current will be turned on again after the scan is completed. Your doctor has access to detailed MRI-related information in the physician's manual.

Patient Magnet is MR Unsafe — Do not carry the patient magnet into the MR scanner room. The magnet could become a dangerous flying object if attracted by the strong magnetic field of the MRI scanner.

Pain or other sensation during MRI scan — If, during an MRI scan, you have any pain, discomfort, heating, or other unusual sensations, notify the MRI operator, so the MR procedure can be stopped.

Cardiac Arrhythmia (Model 106 or 1000 only) — If you have a cardiac arrhythmia, the Automatic Stimulation feature of the Model 106 is not suitable for you. This includes heart conditions or treatments that do not allow necessary changes in your heart rate, such as atrial fibrillation, pacemaker dependency, implantable defibrillator, or cardiac medications such as beta blockers.

4. PRECAUTIONS — IMPLANTABLE DEVICE: GENERAL

Use during pregnancy — The safety and effectiveness of the VNS Therapy System have not been established for use during pregnancy.

Laryngeal irritation may result from stimulation — Patients who smoke may have an increased risk of laryngeal (commonly called the "voice box") irritation.

AutoStim Devices (Model 106 and 1000)

Use during exercise — Exercise or physical activity may trigger Automatic Stimulation if the feature is ON due to heart rate changes detected by the device.

Heart Rate Changes Not Associated with Seizures — Situations, including but not limited to exercise or physical activity, that cause rapid increases in heart rate may trigger Automatic Stimulation if the feature is ON. If this is a concern, talk to your doctor about ways to stop stimulation during these situations. This could include using your magnet or having your doctor turn the AutoStim feature OFF.

Battery Drain — If your doctor has turned on the AutoStim feature, there will be a greater impact on battery life than if the feature is turned off, which may require more frequent generator replacements.

AutoStim follow-up visits — Use of the AutoStim feature will reduce battery life. Once the AutoStim feature has been activated, your doctor will work with you to determine a treatment plan to get to the most benefit.

Time-based Features (Models 1000 only) — Optional time-based features (e.g., Day-Night Programming, Scheduled Programming) do not automatically adjust for Day Light Savings Time or time zone changes. If you are using one of these features, you will need to go back to your doctor for reprogramming of the generator for any time changes.

5. PRECAUTIONS — IMPLANTABLE DEVICE: ENVIRONMENTAL & MEDICAL HAZARDS

Being close to certain types of equipment can affect the generator. Move away from or avoid equipment such as transmitting antennas.

Pacemaker Warning signs — Talk to your doctor before going into places with Pacemaker Warning signs.

Small appliances — Properly operating microwave ovens and other small electrical appliances, such as toasters, hair dryers, and electric shavers, should not affect the generator.

Cellular phones — Cellular phones can affect some implanted cardiac defibrillators and pacemakers, but tests to date show that they do not affect the generator.

Transmitting devices — Properly operating electrical ignition systems and power transmission lines should not affect the generator. Sources with high energy levels, such as transmitting antennas, may interfere with the device. Move at least 1.8 meters (6 feet) away from any equipment that interferes with your device.

Antitheft devices, airport security systems, and other metal detectors — Antitheft devices and metal detectors should not affect the generator or be affected by it. As a precaution, however, move through them at a steady pace; do not linger in the area and stay at least 40 centimeters (16 inches) away from such equipment.

Electronic Article Surveillance (EAS) System tag deactivators — The tag deactivators found in many retail stores can interfere with VNS Therapy when it is used near the generator. It can cause accidental activations or stop pulses. Stay at least 60 centimeters (2 feet) away from tag deactivators to avoid potential interference.

Devices with strong electromagnetic fields — Electrical or electromechanical devices with a strong static or pulsing magnetic field can cause the generator to start suddenly. Such devices may include strong magnets, tablet computers and their covers, hair clippers, vibrators, antitheft tag deactivators, and loudspeakers. Keep this type of equipment at least 20 centimeters (8 inches) away from your chest. If your generator stops while you are in a strong electromagnetic field, move away from the source so the device may return to regular operation.

Medical equipment, procedures, and surgery using certain electrical instruments can affect the VNS Therapy System's operation and sometimes damage the generator or lead.

Make sure that medical personnel know you have a device implanted in your chest.

Always call your doctor before you have any medical tests that may affect, or be affected by, the VNS Therapy System as described in this section. Precautions may be needed.

Routine diagnostic procedures — Most routine diagnostic procedures, such as diagnostic ultrasound and radiography (x-rays), should not affect the VNS Therapy System.

Mammography — Because the generator is in your chest, you may need to be specially positioned for a mammogram. Otherwise, the device may be seen as a shadow on the mammogram. It could make a lesion or lump in that area hard or even impossible to detect. Make sure that your doctor and the mammography technician are aware of the implanted device.

Radiation treatment — Treatment with radiation, cobalt machines, and linear accelerators may damage the generator. No testing has been done to date. The effect of radiation on the device is not known. Talk with your doctor if you plan to have radiation treatment.

Other procedures — External cardiac defibrillation and other procedures for heart problems, as well as extracorporeal shockwave lithotripsy, diathermy, and electrocautery, may damage the generator. If you had any of these procedures and your doctor did not know about it, have the generator checked. While diagnostic ultrasound should not affect the VNS Therapy System, therapeutic ultrasound therapy could damage the generator or inadvertently harm you. While the generator is stimulating or being set or tested, it may briefly interfere with nearby equipment. If this happens, move at least 1.8 meters (6 feet) away from such equipment.

Radios and hearing aids — The generator can interfere with devices that operate in the 30 kHz to 100 kHz range. Hearing aids and transistor radios operate in this range. In theory, the generator could affect them, but no effects have yet been reported. No detailed testing has been done, so the effects are unknown.

Other Implanted devices — The generator may affect other implanted medical devices, such as cardiac pacemakers and implantable defibrillators. Possible effects include sensing problems. These could lead to inappropriate responses from the generator.

6. PRECAUTIONS — MAGNETS

After your operation, your doctor will give you two magnets and accessories. The magnets contain a high-power magnet that is surrounded by a plastic casing in the shape of a watch. With normal use, they should remain powerful for approximately 3 years

Keep magnet with you — Always carry the magnet with you. Show your family members or caregivers how to use it.

Other implanted devices — Do not place the magnet over a pacemaker since it may affect pacemaker function and could change the pacing rate. Do not place the magnet over a defibrillator (sometimes called ICD) since it could turn the device OFF

Damage from magnet — Never put or store the magnets near credit cards, televisions, computers, computer disks, microwave ovens, watches, other magnets or items affected by strong magnetic fields. Keep them at least 25 centimeters (10 inches) away.

If you are not sure how to use the magnet or have questions, ask your doctor to show you how.

7. SIDE EFFECTS

Adverse events reported during clinical studies as statistically significant are listed below in alphabetical order: ataxia (loss of the ability to coordinate muscular movement); dyspepsia (indigestion); dyspnea (difficulty breathing, shortness of breath); hypoesthesia (impaired sense of touch); increased coughing; infection; insomnia (inability to sleep); laryngismus (throat, larynx spasms); nausea; pain; paresthesia (prickling of the skin); pharyngitis (inflammation of the pharynx, throat); voice alteration (hoarseness); vomiting. Adverse events reported in clinical investigation of the AutoStim feature were comparable.

Let's make sure you get the support you need.

Remember to fill out, sign, and return the Patient Information Questionnaire (PIQ) or complete the Patient Authorization Form at VNSPatientForm.com.

For more information, contact your Clinical Nurse Education Specialist or Care Coordinator:
call 1-888-867-7846 or visit VNSTherapy.com

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Brief Summary[1] of Safety Information for the VNS Therapy® System [Epilepsy Indication] (February 2021)

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 patients 4 years of age and older with partial onset seizures that are 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 diathermy on patients implanted with a 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 electrocardiograms and Holter monitoring are 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* chapter of the physician's manuals. 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 (Lead Test) 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 and those with a history of drooling or hypersalivation are at greater risk for aspiration. Use of the magnet to temporarily stop stimulation while eating may mitigate the risk of aspiration.

Dyspnea (shortness of breath) 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 have MRI procedures performed only as described in the *MRI with the VNS Therapy System* instructions for use. In some cases, surgery will be required to remove 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 animals.

Patients who manipulate the generator and lead through the skin (Twiddler's Syndrome) may damage or disconnect the lead from the generator and/or possibly cause damage to the vagus nerve.

The Wand, Programmer, and patient magnet are MR unsafe devices. These devices are projectile hazards and must not be brought into the MR scanner room.

Generators with AutoStim only—The AutoStim Mode feature should not be used in patients with clinically meaningful arrhythmias currently being managed by devices or treatments that interfere with normal intrinsic heart rate responses (e.g., pacemaker dependency, implantable defibrillator, 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)].

Generators with AutoStim only—For anticipated use of the AutoStim feature, it is important to follow the recommended pre-surgical surface assessment described in the Implantation Procedure to determine a location for the generator to reside in which it can accurately detect heart beats

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 by physicians who are trained in surgery of the carotid sheath and have received specific training in the implantation of this device.

The VNS Therapy System is not curative. Physicians should warn patients that the VNS Therapy System is not a cure for epilepsy and that since seizures may occur unexpectedly, patients should 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 (definite, probable, and possible) were recorded 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. Although this rate exceeds that expected in a healthy (nonepileptic) population matched for age and sex, it is within the range of estimates for epilepsy patients not receiving vagus nerve stimulation, ranging from 1.3 SUDEP deaths for the general population of patients with epilepsy, to 3.5 (for definite and probable) for a recently studied antiepileptic drug (AED) clinical trial population similar to the VNS Therapy System clinical cohort, to 9.3 for patients with medically intractable epilepsy who were epilepsy surgery candidates.

5. Precautions — General

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy physician's manuals.

Prescribing physicians should be experienced in the diagnosis and treatment of epilepsy 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 and 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. Children 4-11 years of age may have a greater risk for infection when compared to adolescent and adult patients (≥ 12 years). Careful monitoring for site infection as well as the avoidance of manipulation of the surgical site post implant in children should be stressed.

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

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

Generators with AutoStim only—Because the device senses changes in heart rate, false positive detection may cause unintended stimulation. Examples of instances where the heart rate may increase include exercise, physical activity, and normal autonomic changes in heart rate, both awake and asleep, etc. Adjustments to the AutoStim feature's detection threshold should be considered; which may include turning the feature OFF.

Generators with AutoStim only—The physical location of the device critically affects the feature's ability to properly sense heart beats. Care must be taken to follow the implant location selection process outlined in the Implantation Procedure.

Generators with AutoStim only—Talk to your patient about use of the AutoStim feature since use of the feature will result in faster battery drain and the potential for more frequent device replacements. The physician's manual describes the impacts to the battery life. The patient should return to their physician at appropriate intervals to further evaluate whether they are receiving benefit from the current AutoStim settings.

M1000 only — Since the Scheduled Programming feature allows the generator to apply therapy increases at scheduled intervals, it may not be appropriate for use in patients who are nonverbal or are unable to use the patient magnet to stop undesired stimulation. Similarly, exercise caution for use of this feature in patients with a history of obstructive sleep apnea, shortness of breath, coughing, swallowing difficulties, or aspiration.

6. Environmental and Medical Therapy Hazards

Patients should exercise reasonable caution in avoiding devices that generate a strong electric or magnetic field. If a 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.

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

Therapeutic radiation may damage the 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 generator.

Use of electrosurgery [electrocautery or radio frequency (RF) ablation devices] may damage the generator.

Magnetic resonance imaging (MRI) should not be performed using a transmit RF body coil for certain VNS therapy device configurations or under certain specific conditions. In some cases, heating of the lead caused by the transmit RF body coil during MRI may result in serious injury. Static, gradient, and radio frequency (RF) electromagnetic fields associated with MRI may change the generator settings (i.e., reset parameters) or activate the VNS device if the Magnet Mode output remains "ON". Note that certain magnetic resonance (MR) system head coils operate in receive-only mode and require use of the transmit RF body coil. Other MR systems use a transmit/receive RF head coil. Local or surface coils may also be receive-only RF coils that require the transmit RF body coil for MRI. **The use of a receive RF coil does not alter hazards of the transmit RF body coil.** Exposure of the VNS Therapy System to any transmit RF coil must be avoided. Do not perform MRI scans using any transmit RF coil in the defined exclusion zones. See *MRI with the VNS Therapy System* instructions for use for details or further instructions for special cases such as lead breaks or partially explanted VNS Therapy systems.

Extracorporeal shockwave lithotripsy may damage the generator. If therapeutic ultrasound therapy is required, avoid positioning the area of the body where the 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 generator output to 0 mA for the treatment, and then after therapy, reprogram the 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 generator should be set to 0 mA or function of the generator should be monitored during initial stages of treatment.

Routine therapeutic ultrasound could damage the generator and may be inadvertently concentrated by the device, causing harm to the patient.

For complete information related to home occupational environments, cellular phones, other environmental hazards, other devices, and ECG monitors, refer to the physician's manuals.

7. Adverse Events — Epilepsy

Adverse events reported during clinical studies as statistically significant are listed below in alphabetical order: ataxia (loss of the ability to coordinate muscular movement); dyspepsia (indigestion); dyspnea (difficulty breathing, shortness of breath); hypoesthesia (impaired sense of touch); increased coughing; infection; insomnia (inability to sleep); laryngismus (throat, larynx spasms); nausea; pain; paresthesia (prickling of the skin); pharyngitis (inflammation of the pharynx, throat); voice alteration (hoarseness); vomiting.

[1] The information contained in this Brief Summary for Physicians represents partial excerpts of important prescribing information taken from the physician's manuals. (Copies of VNS Therapy physician's and patient's manuals are posted at www.livanova.com.) 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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