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Health innovation that matters

MIND THE TREATMENT GAP

MEDIA RELEASE

The new campaign to reach thousands of Australians with drug-resistant epilepsy that fall through the treatment gap

- *Around one in three Australians diagnosed with epilepsy have tried two or more appropriately chosen antiseizure medications and still haven't achieved seizure freedom, classifying them as living with drug-resistant epilepsy.[1]*
- *Globally, as many as over 80% of 40% of eligible people living with drug-resistant epilepsy are not receiving alternative treatments to anti-seizure medications to help control their seizures. [2]*

Melbourne, Australia, 19 March, 2024 – A new campaign focused on helping Australians living with drug-resistant epilepsy to better understand available treatment options and access them sooner was launched today.

The campaign, ***Mind the treatment gap,*** asks healthcare professionals and people living with drug-resistant epilepsy to prioritise conversations about treatment pathways alternative to anti-seizure medications to achieve seizure control and improve quality of life. It is supported by leading health experts and consumer advocacy groups as they recognise the stark reality of referral and treatment gaps for people with drug-resistant epilepsy.

Drug-resistant epilepsy is defined as failure of at least two appropriately chosen anti-seizure medications anti-seizure medications to achieve sustained seizure freedom.[3]

Globally, about two-thirds of people with drug-resistant epilepsy are potential candidates for alternative therapies, such as epilepsy surgery, neurostimulation (e.g. vagus nerve stimulation), or dietary therapies.[2] However, only 40% of people with drug-resistant epilepsy have undergone comprehensive evaluation, meaning there is around 60% referral gap.[2] Among those people with drug-resistant epilepsy who have been evaluated, over 80% of people have not received available alternative treatments such as vagus nerve stimulation or surgery.[4] [5] The treatment gap is further exacerbated for people living in regional and rural areas.

The ***Mind the treatment gap campaign*** aims to bridge this gap by educating healthcare professionals on the importance of early referrals to comprehensive epilepsy centres, explaining alternative treatment options for people with drug-resistant epilepsy and building their confidence in having proactive conversations to reduce the timeline from diagnosis to accessing options to improve seizure control.

Carol Ireland, Chief Executive Officer at Epilepsy Action Australia, said despite epilepsy being one of the most common brain disorders, there needs to be stronger awareness of the importance of early referrals to comprehensive epilepsy centres for people with complex epilepsy to bridge the treatment gap.

"Epilepsy as a condition can be frustrating and isolating, especially if the treatment is not delivering the results needed for a better quality of life. We hope that the newly launched Mind the treatment gap campaign will help raise awareness about the gap in our current approach to treatment of people with drug-resistant epilepsy and foster a deeper understanding of this condition and the management it requires," said Ms Ireland.

Dr Michael Fong, MBBS, FRACP an Epilepsy Neurologist at the Westmead Comprehensive Epilepsy Centre in Sydney, said the use of alternative treatment options and referral rate to dedicated epilepsy centres remain low, so conversations around the existing treatment gap are timely and necessary.

"What we see in practice is that it takes people with drug-resistant epilepsy between 3 to 10 years to get a referral to a comprehensive epilepsy centre, with people in regional and rural areas affected the most. We need to increase understanding among general practitioners, neurologists and their patients that there are proven alternative therapies for them to explore earlier in their treatment plan and achieve desired seizure control and quality of life sooner," said Dr Fong.

Despite the introduction of many new anti-seizure medications over the past 30 years, including some with novel mechanisms of action, seizure freedom rates have stagnated.[6 7 8 9 10]

This reinforces the need for increased awareness and use of alternative treatment options for people with drug-resistant epilepsy, including options like epilepsy surgery, vagus nerve stimulation therapy (VNS Therapy™), deep brain stimulation, ketogenic diet, and potential epilepsy precision therapies.[11]

VNS Therapy™ is an adjunctive neuromodulation therapy widely used to reduce seizure frequency in people with drug-resistant epilepsy who are not suitable for resective surgery.[12 13] It works by delivering mild pulses to the vagus nerve at regular intervals throughout the day via a small device implanted under the skin to reduce seizure frequency and improve recovery time.[14] In Australia, this therapy is an option for patients with drug-resistant epilepsy alongside other treatment options at comprehensive epilepsy centers. VNS Therapy™ is indicated for use as an adjunctive therapy in reducing the frequency of seizures in patients whose epileptic disorder is dominated by partial seizures (with or without secondary generalization) or generalized seizures that are refractory to seizure medications.

Key statistics about drug-resistant epilepsy

- Six in ten (60%) Australians are not aware of drug-resistant epilepsy.[1]
- Only 42% of Australians are aware of at least one alternative treatment (surgery, diet, VNS Therapy™, and other treatments).[1]
- Uncontrolled seizures increase risk of premature death up to 10 times.[14]
- People with uncontrolled seizures incur eight times greater financial cost than those with controlled epilepsy.[14 15]
- There are approximately 29,000 people living with drug-resistant epilepsy in Australia who are not suitable for surgery or failed to achieve seizure control following surgery.[16]
- in 2023, only about 0.5% of eligible people have been treated with VNS Therapy™.[16]

Professor Piero Perucca, MD, PhD, FRACP, the Director of the Bladin-Berkovic Comprehensive Epilepsy Program at Austin Health and a global leader in research in the diagnosis and management of epilepsy, says early identification and referral of people with drug-resistant epilepsy to comprehensive epilepsy centres allows for effective treatment that may reduce mortality and the potentially irreversible psycho-social consequences of continuing seizures.

"There is an urgent need to address the treatment gap among people with drug-resistant epilepsy as the likelihood of achieving seizure control diminishes with each unsuccessful anti-seizure medication trial. Fortunately for Australians, there are comprehensive epilepsy centres in nearly every state, allowing for people with drug-resistant epilepsy to be referred without delays to optimise their treatment plan," said Professor Perucca.

Epilepsy experts recommend that Australians with drug-resistant epilepsy should be referred to comprehensive epilepsy centres for diagnostic, re-evaluation and targeted management as soon as possible to optimise their treatment response. These centres are best equipped

to evaluate people that are not responding to anti-seizure medications and have better chances at bridging the treatment gap.

To support Mind the treatment gap campaign and access useful resources about drug-resistant epilepsy, visit www.vnstherapy.com.au

For information about epilepsy and support services, visit Epilepsy Action Australia: https://www.epilepsy.org.au

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About LivaNova

LivaNova PLC is a global medical technology company built on nearly five decades of experience and a commitment to improve the lives of patients around the world. LivaNova's advanced technologies and innovative treatments provide meaningful solutions for the benefit of patients, healthcare professionals and healthcare systems. Headquartered in London, LivaNova has a presence in more than 100 countries worldwide. For more information, please visit livanova.com.

References

[1] YouGov. (2023). LivaNova epilepsy consumer research survey. [data on file].
[2] Boon P, et al Eur Neurol Rev. 2015;10:171–5.
[3] Kwan P et al, Definition of drug resistant epilepsy, Epilepsia, 51(6):1069–1077, 2010 doi: 10.1111/j.1528-1167.2009.02397.x
[4] Boon P, et al Eur Neurol Rev. 2015;10:171–5.
[5] Data on file as a result of multiple surveys made during LivaNova education events.
[6] Kwan P, et al. N Engl J Med 2000;342:314-9
[7] Mohanraj R et al. Eur J Neurology. 2006; 13:277-282.
[8] Brodie, MJ, et al. Neurology. 2012; 78:1548-1554.
[9] Chen Z, et al. JAMA Neurol 2017. doi10.1001/jamaneurol.2017.3949.
[10] Perucca E, Perucca P, White HS, Wirrell EC.Drug resistance in epilepsy. Lancet Neurol. 2023 Aug;22(8):723-734
[11] Epilepsy Action Australia. Medication resistant epilepsy, accessed February 2024 at https://www.epilepsy.org.au/about-epilepsy/managing-epilepsy/medication-resistant-epilepsy/
[12] Elliott RE, et al. Epilepsy Behavior 2011;20(1):57-63.
[13] VNS Therapy, What does VNS Therapy involves, accessed September 2021 at https://vnstherapy.com/learn-more/how-it-works
[14] VNS Therapy System Physician's Manual Australia (M1000), July 2020; 47
[14] Alexopoulos AV. Epileptology 2013;1:38–42;
[15] Strzelczyk A, et al. Front Neurol. 2017;8:712.
[16]Data on file, LIvaNova PLC, Houston , TX.

Brief Summary of Safety Information for Patients
VNS Therapy™ System [Epilepsy Indication] (December 2022)

1. INDICATIONS

The VNS Therapy System (exclusive of SenTiva™) is indicated for use as an adjunctive therapy in reducing the frequency of seizures in patients whose epileptic disorder is dominated by partial seizures (with or without secondary generalization) or generalized seizures that are refractory to seizure medications. AspireSR™ features an Automatic Stimulation Mode which is intended for patients
who experience seizures that are associated with cardiac rhythm increases known as ictal tachycardia.
The SenTiva™ pulse generator 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 (with or without secondary
generalization) or generalized seizures that are refractory to antiepileptic medications. SenTiva features an Automatic Stimulation Mode which is intended for patients who experience seizures that are
associated with cardiac rhythm increases known as ictal tachycardia.

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; progressive neurological diseases other than epilepsy or depression.
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.

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