AspireSR®
Empowers patients with seizure detection and automatic stimulation both night and day

The first choice add-on in drug-resistant epilepsy
Drug-Resistant Epilepsy:
A complex disease needs a comprehensive approach

VNS Therapy®:
• Can be used in combination with other approved treatments at any time
• Helps you to meet therapy goals and restore patient wellness
AspireSR detects and responds to seizures 24/7 to improve the lives of patients with epilepsy

AspireSR uses unique technology that detects seizures based on changes in heart rate and provides automatic stimulation to stop or shorten a seizure and improve postictal recovery.

- **AspireSR** is proven in 2 clinical trials to reduce seizure frequency, severity, and duration, and improve quality of life outcomes.¹
- **AspireSR** advances the proven foundation of VNS Therapy® and offers a comprehensive approach for people living with drug-resistant epilepsy.
- **AspireSR** has demonstrated safety and tolerability comparable to currently available VNS Therapy.
- **AspireSR** provides 24/7 seizure detection and automatic stimulation. Patients can still use a handheld magnet for added control and confidence.
How AspireSR works

• Detects heart rate increases associated with seizures
• Delivers automatic stimulation
• Has customisable parameters to meet patients’ needs
• Works in conjunction with normal and magnet mode

82% of patients with epilepsy have seizure-associated tachycardia\(^1\)
AspireSR provides 24/7 seizure detection and automatic stimulation

AspireSR may terminate seizures by delivering automatic stimulation when a seizure occurs\(^1\)

- Over 60% of seizures treated (n=46) ended during automatic stimulation\(^1\)
  - 48% of Complex Partial Seizures ended during automatic stimulation
- For seizures that ended during stimulation (n=28), the closer stimulation was to seizure onset, the shorter the seizure duration\(^1\)

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**STIMULATION-ASSOCIATED DESYNCHRONIZATION DURING FOCAL SEIZURE* (N=46 TREATED SEIZURES)**

Threshold for automatic stimulation = 20% heart rate rise for this patient.

\(^*\)Individual study patient example. Results may vary.
The handheld patient magnet helps empower patients to **stop or shorten seizures**²

Magnet use allows patients to stop or shorten a seizure, or decrease the intensity of the recovery period.

Robert on VNS Therapy since 2006

**POSITIVE IMPACT**  
(5,849 SEIZURES)

- 62% Seizures terminated 2,211
- 38% Seizures diminution 3,638

**SEIZURE NOT AFFECTED**  
(3,633 SEIZURES)

- 62% Seizures uneffected 3,633

Morris 2003²

Of seizures are terminated or diminished when the magnet is used²
Many seizures are missed during sleeping hours

Records of over 10 million magnet activations since 1997 approval show that activations are far less common between midnight and 6 am.

Handheld magnet activation is not always convenient:

- Would not be able to perform manual magnet mode stimulation
- Do not have a magnet available when needed
- Do not apply magnet properly (at the wrong time or wrong device location)
- May not have enough time to apply the magnet once the seizure starts
- Do not experience auras
- Do not have a caregiver, or caregiver may not be near when patient is having a seizure
- Have a seizure during a period of sleep

91% of patients surveyed would value a device that can automatically activate stimulation.
AspireSR is proven to reduce seizure severity\textsuperscript{1,4}

Sustained improvements in seizure severity were seen across multiple validated scales scored by patients and physicians:

- Seizure Severity Questionnaire (SSQ) – Clinically meaningful and statistically significant change in overall seizure severity and recovery were seen at 3 and 12 months\textsuperscript{4}

**SSQ SCORE: MEAN CHANGE FROM BASELINE\***

![SSQ Score Diagram](image)

**NHS3 SCORE: MEAN CHANGE FROM BASELINE**

![NHS3 Score Diagram](image)

- National Hospital Seizure Severity Scale (NHS3) – Statistically significant reductions in seizure severity were observed after 3–5 days of only automatic stimulation in the EMU and at 12 months\textsuperscript{1}

\*Using normalized data.  †Statistically significant (P<0.05).

No EMU discharge data available since SSQ has a 30 day recall period
AspireSR is proven to improve quality of life\(^4\)

Clinically meaningful and statistically significant improvements in overall QOL were seen at 3 months and continued to improve over time.

### QUALITY OF LIFE (QOLIE-31-P) SCORE: MEAN CHANGE FROM BASELINE*

<table>
<thead>
<tr>
<th></th>
<th>3 months</th>
<th>12 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>QOL OVERALL TOTAL</td>
<td>1.3(^†)</td>
<td>2.1(^†)</td>
</tr>
<tr>
<td>OVERALL QUALITY OF LIFE</td>
<td>1.0(^†)</td>
<td>2.2(^†)</td>
</tr>
<tr>
<td>SOCIAL FUNCTIONING</td>
<td>2.9(^†)</td>
<td>3.9(^†)</td>
</tr>
<tr>
<td>COGNITIVE FUNCTIONING</td>
<td>1.6(^†)</td>
<td>2.2(^†)</td>
</tr>
<tr>
<td>SEIZURE WORRY</td>
<td>1.1(^†)</td>
<td>1.8(^†)</td>
</tr>
<tr>
<td>EMOTIONAL WELL-BEING</td>
<td>0.8</td>
<td>1.8(^†)</td>
</tr>
<tr>
<td>MEDICATION EFFECTS</td>
<td>1.4</td>
<td>1.0</td>
</tr>
<tr>
<td>ENERGY/FATIGUE</td>
<td>0.5(^†)</td>
<td>1.2</td>
</tr>
</tbody>
</table>

\(^†\) Statistically significant (P<0.05).

\(^*\) Using normalized data.

\(^4\) Clinically Meaningful Change

N=48, 47, 46, 48, 48, 47, 47
AspireSR provides seizure reduction that continues to improve over time\(^1\)

Of patients in AspireSR trials:
- 90% failed 4 or more anti-epileptic drugs
- Mean duration from diagnosis was 23 years
- Approximately 35% of patients had a prior resective surgery

**SUMMARY OF RESPONDER RATE**

**E-36 Clinical Trial : Europe, N=31**
- During the EMU stay, patients were randomized to 3 different AutoStim threshold settings
- After the EMU stay, investigators adjusted the threshold for AutoStim using their discretion

**E-37 Clinical Trial : US, N=20**
- During the EMU stay, investigators set the threshold for AutoStim using their discretion
- Duty cycle held at 10% through 6 month follow-up to isolate the effect of the AutoStim feature.

**AspireSR is proven to reduce seizure duration\(^1\)**

Complex Partial Seizures that were treated with Automatic Stimulation were at least 34% shorter than historical seizures of the same type\(^1\)

**COMPLEX PARTIAL SEIZURES**

<table>
<thead>
<tr>
<th>Median seizure duration (seconds)</th>
<th>n= number of seizures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Historical Seizures</td>
<td>83 sec N=108</td>
</tr>
<tr>
<td>Seizures Terminated During Stimulation</td>
<td>55 sec N=11</td>
</tr>
</tbody>
</table>

Median duration of seizures by subgroup

Median seizure duration was at least 34% shorter than historical seizures of the same type.
AspireSR® Advancing the proven long-term efficacy and safety platform of VNS Therapy

VNS Therapy with AspireSR benefits:¹

- Provides the proven long-term efficacy and safety of VNS Therapy
- Uses a proprietary, customisable cardiac-based seizure detection algorithm to deliver stimulation when a seizure occurs
- May terminate seizures by delivering automatic stimulation when a seizure occurs
- Reduces seizure duration
- Reduces seizure severity
- Improves Quality of Life

AspireSR® is CE mark approved and commercial distribution may vary by country.

VNS THERAPY EUROPEAN INDICATION FOR USE

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. The Model 106 AspireSR® Seizure Response (Mode) features the Automatic Stimulation Mode, which is intended for patients who experience seizures that are associated with cardiac rhythm increases known as ictal tachycardia.

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 the VNS Therapy system. Diagnostic ultrasound is not included in this contraindication. Cardiac arrhythmia should not be used in patients with clinically meaningful arrhythmias or who are using treatments that interfere with normal intrinsic heart rate responses.

warnings:

Physicians should inform patients about all potential risks and adverse events discussed in the VNS Therapy Physician Manuals, including information that VNS Therapy may not be a cure for epilepsy. Since seizures may occur unexpectedly, patients should consult with a physician before engaging in unsupervised activities, such as driving, swimming, and bathing, or in strenuous sports that could harm them or others. A malfunction of the VNS Therapy system could cause painful or direct current stimulation, which could result in nerve damage. Removal or replacement of the VNS Therapy system requires an additional surgical procedure. Patients who have pre-existing swallowing, cardiac, or respiratory difficulties (including, but not limited to, obstructive sleep apnoea and chronic pulmonary disease) should discuss with their physicians whether VNS Therapy is appropriate for them since there is the possibility that stimulation might worsen their condition. Postoperative bradycardia can occur among patients with certain underlying cardiac arrhythmias. MRI can be safely performed; however, special equipment and procedures must be used.

ADVERSE EVENTS:

The most commonly reported adverse events from stimulation include hoarseness (voice alteration), paresthesia (prickling feelings in the skin), dyspnea (shortness of breath), sore throat and increased coughing. The most commonly reported adverse event from the implant procedure is infection.

*The information contained here represents partial excerpts of important prescribing information from the product labeling. Patients should discuss the risks and benefits of VNS Therapy with their healthcare provider. Visit www.VNSTherapy.com for more information.

References:

1. Data on file, Cyberonics Inc. Houston, TX
3. Eggleston et al. 2014 Aug;23(7):496-505
4. Adapted from data on file, Cyberonics Inc. Houston, TX.

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