Introducing PoNS™ (Portable Neuromodulation Stimulator)

PoNS Treatment™:
Restoring balance and gait through noninvasive neuromodulation

The PoNS™ device is intended for use as an acute treatment of chronic balance deficit due to mild-to-moderate traumatic brain injury (mmTBI), and is to be used in conjunction with physical therapy (PT). The device is limited to prescription use.

Contraindications
The PoNS™ device delivers electrical stimulation directly to the surface of the tongue. Precautions for use are similar to those for transcutaneous electrical nerve stimulation (TENS). Electrical stimulation SHOULD NOT be used: if there is an active or suspected malignant tumor, in areas of recent bleeding or open wounds, or in areas that lack normal sensation. PoNS™ has not been tested on, and thus should not be used by, individuals under the age of 18 or who are pregnant. PoNS™ should not be used in patients sensitive to nickel, gold, or copper.

PoNS™ is an authorized medical device and commercially available in Canada. PoNS™ is an investigational device under review for EU clearance by an EU notified body and by TGA in Australia; PoNS™ is not commercially available in the US, EU, or Australia.
Chronic balance deficit is prevalent\(^5-8\)

\(~350\) THOUSAND people in Canada are living with chronic balance deficit after an mmTBI\(^5-7\)

\(~13\) THOUSAND new cases of chronic balance deficit from mmTBI are reported annually in Canada\(^6-8\)

Rehabilitation therapy (physical therapy, occupational therapy, and vestibular therapy) is the current standard of care.\(^9\)

However, 10\%-40\% of patients plateau or lose functions gained from rehabilitation therapy\(^7,9-11\)
In patients who have experienced an mmTBI

The moment of impact can have a lasting effect\textsuperscript{9,11,12}

- Chronic balance deficit often has a significant negative impact on functional status, capacity to return to work, and quality of life

- Dizziness/coordination\textsuperscript{11}
- Difficulty walking\textsuperscript{11}
- Trouble climbing stairs\textsuperscript{11}
- Difficulty completing everyday tasks\textsuperscript{11}
- High risk of falling\textsuperscript{12}

When symptoms persist, evidence indicates that neurostimulation combined with physical therapy can potentially affect rehabilitation outcomes\textsuperscript{9,13}
PoNS Treatment™ provides an innovative and effective therapy\textsuperscript{1}

\begin{itemize}
\item The device is portable and simple to use, with software to capture patient adherence
\item During each 20-minute session, the patient places a paddle-shaped mouthpiece on the tongue and wears a controller around the neck. Patients feel a mild sensation while using the device
\item Patients have complete control over the intensity throughout the training
\item PoNS Treatment™ is conducted by PoNS™ Trainers—rehabilitation therapists who complete specialized training through a certification course
\end{itemize}

\textbf{Warnings}

\textit{The intensity should only be adjusted while the Mouthpiece is on the tongue. The patient should be the one who adjusts the intensity level. In case the patient needs assistance in pressing the buttons on the Controller, the person assisting should use care to adjust the intensity by small increments. Check with the patient each time you press the INTENSITY UP/DOWN buttons, before pressing them again.}
PoNS Treatment™ is believed to promote neuroplasticity\textsuperscript{14,15}

How it works

- PoNS Treatment™ combines mild stimulation of the tongue with targeted training\textsuperscript{1}
- Translingual stimulation of the trigeminal and facial nerves initiates a cascade of neural activity, resulting in neuromodulation\textsuperscript{14,15}
- Multiple sequential training sessions lead to reduction of symptoms\textsuperscript{1,14,15}
- The combination of stimulation with targeted training may enhance the neuroplastic effect, which results in functional improvements in balance and gait\textsuperscript{14}

PoNS™ is for use by a single individual and must not be shared.

Visit www.ponestreament.ca for more information.
PoNS™ was studied in conjunction with targeted physical therapy in 2 clinical trials involving 163 patients.

Both trials used the same criteria to enroll a challenging patient population, defined as:

- **Were ≥1 year post-injury**
- **Deemed to have plateaued with previous PT**
- **Sensory Organization Test (SOT) ≥16 points below normal (composite score)**

**Use with caution**

*Electrical stimulation should only be used after seeking professional medical advice, and with caution in patients with any of the following:*

- Implanted electronic devices, including: cardiac pacemakers, cardioverter defibrillators, deep brain stimulators, vagal nerve stimulators, sacral nerve stimulators, and cochlear implants
- Metal in the mouth (e.g. piercings, braces, retainers, or other orthodontic appliance)
- Seizure disorders
- Epilepsy
Additional criteria

- Patient inclusion criteria: age 18-65; balance disorder as a result of mmTBI†; ≥1 year since their TBI; deemed by themselves or their HCP to have plateaued in recovery with their PT program; SOT composite scores ≥16 points below normal after adjustment for their age and height.

- Patient exclusion criteria: history of TBI due to disorders unrelated to TBI; penetrating injury, craniotomy, or subdural hematoma; oral health problems or history of oral cancer; other causes for balance disorder.

Both trials had a high-frequency pulse (HFP) and low-frequency pulse (LFP) stimulation arm, in conjunction with PT

- The HFP device is commercially available in Canada.

SOT endpoint was measured by NeuroCom® SOT composite score. SOT is a validated, objective measure of balance

- SOT measures and evaluates somatosensory, visual, and vestibular components of balance. A composite score is then calculated and compared with a database that takes age and height into account.

- SOT scores range from 0-100, with ≥70 considered normal.

- A change of 8-10 points is considered clinically meaningful.

*Defined as mild to moderate by the Armed Forces Health Surveillance Branch.
There were 2 consecutive stages: in-clinic treatment and at-home treatment

2 weeks IN CLINIC (with PoNS Treatment™) → 3 weeks AT HOME (with PoNS Treatment™)

- Performed at 7 centers in the US and Canada
- On average, patients were 5.7 years post-injury and completed 8.8 months of prior PT
- Baseline SOT score was 41.6

The primary endpoint was percentage of responders after 5 weeks of training

- There was no statistical difference between the groups with regard to percentage of responders, as with many trials comparing HFP vs LFP stimulation
- The statistical analysis plan accounted for this possibility and specified combining the groups if this occurred

In patients with chronic balance deficit due to mmTBI

TBI-001 Trial: A 5-week, multicenter study in 120 patients

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- The statistical analysis plan accounted for this possibility and specified combining the groups if this occurred
At 5 weeks, the pooled analysis showed a significant 67.2% of patients responding to treatment\textsuperscript{19,20}

Secondary endpoints\textsuperscript{2}

• PoNS Treatment™ also demonstrated statistically significant improvements in SOT change from baseline, Dynamic Gait Index scores, and the 6-Minute Walk Test from baseline to Week 2 and Week 5

Important Information

Please see page 13 for TBI-001 Trial safety information.

Visit www.ponstreatment.ca for more information.
In patients with chronic balance deficit due to mmTBI

Long-Term Treatment Trial: A 26-week study in 43 patients

There were 3 consecutive stages: in-clinic treatment, at-home treatment, and a follow-up without treatment

2 weeks IN CLINIC (with PoNS Treatment™) 12 weeks AT HOME (with PoNS Treatment™) 12 weeks FOLLOW-UP (without PoNS Treatment™)

- On average, patients were 6.5 years post-injury and completed 5.4 months of prior PT
- Baseline SOT score was 39.6

The primary endpoint was change in SOT composite score from baseline to Week 14

There were significant improvements in SOT score from baseline to each timepoint for both treatment groups ($P<0.0001$)

- There was no statistical difference between the HFP and LFP stimulation groups
Results from a post hoc analysis combining both arms in the Long-Term Treatment Trial

PoNS Treatment™ significantly improved patients’ SOT balance scores

At Week 14, SOT composite scores improved by 31.8—more than 3x the results shown in studies using conventional physical therapy.

PoNS Treatment™ significantly improved patients’ SOT balance scores

Nearly 70% of patients responded at Week 14 (P<0.0001)

≥15 points= definition of responder in this study

8-10 points= clinically meaningful change

IMPROVEMENTS PERSISTED for at least 12 WEEKS after the treatment period (Weeks 14-26)

Visit www.ponstreatment.ca for more information.
PoNS Treatment™ also demonstrated significant improvements in gait\(^4\)

Secondary endpoints

- **Dynamic Gait Index (DGI)** – Assesses gait, balance, and fall risk during walking when presented with challenging obstacles
  - 3 points is considered a clinically meaningful change\(^{21}\)

![](chart.png)

A higher DGI score indicates a lower fall risk

- **6-Minute Walk Test (6MWT)** – Measures walking speed

![](chart.png)
Noninvasive PoNS Treatment™ was shown to be well tolerated\textsuperscript{2,3}

\textbf{TBI-001 Trial}\textsuperscript{2}

- 22 device-related adverse events (AEs) were reported across 12 patients. The most common were burning sensation on the tongue (6), tongue tingling (4), sore tongue (3), and decrease in tongue sensation (2). All were mild.

- 24 severe treatment-related AEs were reported across 9 patients. The most common were nausea (5), vomiting episode (multiple) (5), worsening nausea (2), and fainting episode (2). None were deemed to be device-related.

\textbf{Long-Term Treatment Trial}\textsuperscript{3}

- 2 mild device-related AEs were reported across 2 patients (prickly sensation on tongue; numb sensation on tongue and food taste disturbance).

- There were no severe treatment-related AEs reported.

Excess salivation during training sessions often occurs but generally improves as patients get used to wearing the mouthpiece.\textsuperscript{3,19}

All safety endpoints were met with PoNS Treatment™ in clinical trials\textsuperscript{9,19}
Getting patients back to the moments that matter most

Daily PoNS Treatment™ schedule (6 days a week)

<table>
<thead>
<tr>
<th>Morning session</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Warm-up exercises</strong></td>
<td>10 min</td>
</tr>
<tr>
<td><strong>Balance training with PoNS™</strong></td>
<td>20 min</td>
</tr>
<tr>
<td><strong>Gait training with PoNS™</strong></td>
<td>20 min</td>
</tr>
<tr>
<td><strong>Breathing awareness training with PoNS™</strong></td>
<td>20 min (for first 2 weeks)</td>
</tr>
<tr>
<td><strong>BREAK</strong></td>
<td>3 TO 4 HRS</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Afternoon session</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Balance training with PoNS™</strong></td>
<td>20 min</td>
</tr>
<tr>
<td><strong>Movement control exercises</strong></td>
<td>20 min</td>
</tr>
<tr>
<td><strong>Gait training with PoNS™</strong></td>
<td>20 min</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Evening session</th>
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<tbody>
<tr>
<td><strong>Breathing awareness training with PoNS™</strong></td>
<td>20 min</td>
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</tbody>
</table>

- Home training (12 weeks) requires 1 weekly morning or afternoon session in the clinic

In the Long-Term Treatment Trial (26 weeks), almost all of the patients (91%) participating completed the 14-week PoNS Treatment™.
Evaluate and treat with PoNS™ and PT

Call 833-613-1175 for support, device purchase or replacement, or payment questions.

Visit www.ponstreatment.ca for more information.
PoNS Treatment™ is the first noninvasive neuromodulation therapy of its kind\(^1\)

An innovative and effective treatment for patients with chronic balance deficit due to mmTBI\(^3,4\)
- Efficacy was shown in a challenging patient population: patients $\geq$1 year post-injury who were deemed to have plateaued in recovery with prior PT
- Nearly 70% of patients responded at Week 14 ($\geq$15 points = definition of response; 8-10 points = clinically meaningful change)
- Improvements persisted for at least 12 weeks after the treatment period ended

Shown to be well tolerated in 2 clinical trials\(^2,3\)

Important Information
Please see page 13 for clinical trial safety information.

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References:

Visit www.ponstreatment.ca for more information.

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