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Nevro Turns To Clinical Evidence To Attract Doctors, Patients And Reimbursement For Pain Therapy

by Reed Miller

The FDA recently approved Nevro's Senza high-frequency spinal cord stimulation systems to treat pain caused by diabetic neuropathy. Now it plans to expand its proprietary HFX high-frequency treatment to more indications.

Nevro Corp. is relying on compelling clinical data to drive adoption of its Senza line of spinal cord stimulation systems delivering its proprietary HFX (high-frequency) 10 kHz spinal cord stimulation therapy.

The US Food and Drug Administration approved the original version of Senza in 2015 based on results of the *SENZA RCT* trial, which showed HFX therapy provides long-term improvements in quality of life and functionality for people with chronic low-back pain and leg pain.

In July, Senza became the first spinal cord stimulation system specifically approved by the FDA to treat painful diabetic neuropathy (PDN). That indication expansion is supported by *SENZA-PDN*, the largest randomized trial of spinal-cord therapy to treat PDN. *Six-month results* from SENZA PDN showed that PDN patients treated with HFX and medical therapy were significantly more likely to respond to therapy than patients treated with drug therapy only. (Also see "*NANS 2021: Nevro's HF10 Spinal-Cord Stimulator Succeeds In Two Trials*" - Medtech Insight, 19 Jan, 2021.)

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> *therefore, who is struggling with a lot of bad outcomes." – Keith Grossman*

“We've got a population that needs help [and] we think we've got a technology that can offer them that help and maybe offer them that help uniquely,” Nevro CEO Keith Grossman told *Medtech Insight*. “The challenge is now we've got to go out and help them find these patients and refer them to the pain community.”

Since 2015, most of Nevro’s customers were pain specialists, but these physicians rarely treat PDN patients because there are no other effective therapies to treat PDN. Now that the FDA has approved the PDN indication, Nevro can market Senza to PDN patients directly and to the doctors who treat PDN patients, including primary care physicians, endocrinologists, and podiatrists who treat foot pain.

“They're kind of spread out all over the place,” he said. “We've got to get to these patients and to these referring doctors. And that's what we're in the process of doing.”

Grossman said the company has been able to identify physicians who treat a lot of PDN patients by tracking prescriptions for pregabalin, a common medication for PDN, marketed by Pfizer as Lyrica.

“So, it's kind of a breadcrumb trail. We know who is treating a lot of these patients and, therefore, who is struggling with a lot of bad outcomes,” he said. “And that's who we're going to first, the largest of these practices to treat the most patients.”

Supporting Adoption With Clinical Data

In addition to the unique FDA-approved indication, HFX therapy is supported by a growing body of clinical evidence that Nevro can leverage to support physician-referral decisions.

The full 12-month results from SENZA PDN, showed that HFX therapy caused significant, durable improvements in pain symptoms and neurological function in patients with persistent PDN. These results are now published in *Diabetes Care*.

At 12 months, 86% of the 113 trial subjects randomized to treatment with HFX reported at least a 50% improvement in pain relief as measured by the visual analog score. The average improvement was 77.1%. None of the devices in the trial had to be explanted due to loss of efficacy, but 3.2% of the devices had to be taken out after becoming infected.

The trial design also allowed patients originally assigned to medical therapy only to "crossover" to treatment with HFX after six months and 64 of these patients received a Senza implant. Six months later, 84% of the crossover group reported at least 50% pain relief with an average pain-relief improvement of 70.3%.

Results of a separate study of HFX therapy in 89 "real-world" PDN patients followed for an average of 21.8 months showed that almost 80% of patients responded to the therapy. Results of the study, led by Jeffrey Chen of the University of California, San Diego were recently published in the *Journal of Diabetes Science and Technology*.

> ***"There are no pharmacological treatments out there and no other devices that have demonstrated improved neurological function [in PDN patients], and if we could show disease modification … that would be a big step forward." – David Caraway***

SEZNA PDN also showed improvement in investigator-assessed neurological function outcomes – including lower limb motor strength, sensory function, and reflexes – in 68% of the patients treated with HFX for 12 months. Also, 62% of the crossover patients in the trial showed improvement in investigator-assessed neurological outcomes after six months of treatment.

David Caraway, Nevro's chief medical officer, told Medtech Insight that these neurological outcomes are especially "tantalizing and exciting" because most PDN patients have progressive neurological deficits.

Caraway said the company is sponsoring further research on how to maximize the neurological benefits of HFX, especially the improvement in extremity sensitivity.

"Many of these patients, once they lose [feeling in their extremities] start getting cuts that are unknown to them, which get infections, end up in amputations, and cause a huge burden on the system [and] a tremendous loss of quality of life to the patient," he explained.

He said the company has assembled a group of advisors, including top diabetologists, "to make sure that we're looking at the most impactful measures of improvement in neurological function." This research will include objective measures of the therapy's effect, including biopsies to assess nerve-fiber density, and nerve conduction studies.

“There are no pharmacological treatments out there and no other devices that have demonstrated improved neurological function [in PDN patients], and if we could show disease modification … that would be a big step forward. So that's exciting for us.”

A health economic analysis of the SENZA PDN trial showed that HFX therapy reduced PDN patients’ hospitalization rates and length of stay in patients in the first six months of therapy. Naomi Sacks of Precision Health Economics in Boston presented that analysis at the International Society for Pharmacoeconomics and Outcomes Research (ISPOR) Europe 2021 virtual meeting in late November.

Caraway pointed out that studies like these can help secure reimbursement from commercial payers.

HFX has “broad coverage” but reimbursement for HFX therapy for PDN patients among commercial insurers is “mixed,” he said. “We're gaining every day and we're working with most of the commercial payers to get a reliable coverage, and that's done by giving them compelling data.”

Nevro Seeks Non-Surgical Back Pain Indication

Nevro also plans to market Senza to patients suffering "non-surgical refractory back pain,” which is a form of chronic and debilitating back pain in patients who are not considered good candidates for spine surgery.

Caraway explained that insurers could cover HFX for non-surgical back pain treated under the current FDA-approved label, but that many of them will not cover it until they see compelling clinical trial data.

> ***Nevro's PMA supplement for non-surgical refractory back pain is “on track” to be approved by the end of 2021 or in early 2022.***

Nevro is supported by SENZA NSRBP, a 211-patient randomized trial comparing conventional medical management plus HFX therapy with Senza to medical management alone in patients with non-surgical refractory back pain. One-year results from the trial will be presented on 15 January at the 2022 North American Neuromodulation Society Annual Meeting by Leonardo Kapural from Carolinas Pain Institute in Winston-Salem, NC.

Three-month results of the trial, presented by Kapural at the 2021 NANS conference, showed 80.9% of patients treated with HFX and medication responded to the therapy versus just 1.3% of the patients treated with medication alone. The patients in the HF10 group improved an average of 24 points on the 100-point Oswestry Disability Index while the patients in the medication-only group showed almost no change in disability scores.

In August, Nevro submitted a premarket approval (PMA) supplement to the FDA based on the SENZA NSRBP data, asking the agency to expand Senza's approved labeling to include non-surgical refractory back pain. During Nevro's third-quarter 2021 sales and earnings call on 8 November, Grossman said that PMA supplement is "on track" to be approved by the end of 2021 or in early 2022.