NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Centre for Health Technology Evaluation

Review Decision

Review of MTG41: Senza spinal cord stimulation system for delivering HF10 therapy to treat chronic neuropathic pain

This guidance was issued in January 2019.

NICE proposes an amendment of published guidance if there are no changes to the technology, clinical environment or evidence base which are likely to result in a change to the recommendations. However, the recommendations may need revision to correct any inaccuracies or to update to current formats. The decision to consult on an amendment of published guidance depends on the impact of the proposed amendments and on NICE's perception of their likely acceptance with stakeholders. NICE proposes an update of published guidance if the evidence base or clinical environment has changed to an extent that is likely to have a material effect on the recommendations in the existing guidance.

1. Recommendation

No change to the current guidance.

Do not consult on the review proposal.

Please see Appendix 1 for a list of the options and their explanations for consideration

2. Original objective of guidance

To assess the clinical and cost effectiveness of Senza spinal cord stimulation system for delivering HF10 therapy to treat chronic neuropathic pain.

3. Current guidance

1.1 The case for adopting Senza spinal cord stimulation (SCS) for delivering HF10 therapy as a treatment option for chronic neuropathic back or leg pain after failed back surgery is supported by the evidence. HF10 therapy using Senza SCS is at least as effective as low-frequency SCS in reducing pain and functional disability, and avoids the experience of tingling sensations (paraesthesia).

1.2 Senza SCS for delivering HF10 therapy should be considered for patients:

- *with residual chronic neuropathic back or leg pain (at least 50 mm on a 0 mm to 100 mm visual analogue scale) at least 6 months after back surgery despite conventional medical management and*

- *who have had a successful trial of stimulation as part of a wider assessment by a multidisciplinary team.*

1.3 Patients with other causes of neuropathic pain were included in the evaluation and may be considered for HF10 therapy using Senza SCS but any additional benefits compared with low-frequency SCS are less certain. Cost modelling indicates that, over 15 years, HF10 therapy using Senza SCS has similar costs to low-frequency SCS using either a rechargeable or non-rechargeable device.

1.4 Clinicians implanting SCS devices including Senza should submit timely and complete data to the UK Neuromodulation Registry.

1.5 When assessing the severity of pain and the trial of stimulation, the multidisciplinary team should be aware of the need to ensure equality of access to treatment with SCS. Tests to assess pain and response to SCS should take into account a person's disabilities (such as physical or sensory disabilities), or linguistic or other communication difficulties, and may need to be adapted.

4. Rationale

The original guidance recommended Senza for use in neuropathic back or leg pain after failed back surgery. In this guidance review, clinical evidence relevant to the scope of the guidance and published since the original guidance was reviewed. The aim of the review is to explore if:

- there is new evidence which does not align with the current recommendations
- there is new evidence to support updating the current guidance to include any population sub-groups that did not previously receive a positive recommendation.

Newcastle External Assessment Group (EAG) carried out the evidence review and concluded that there is nothing in the new evidence that would support a change to the existing recommendations. The evidence review report contains further details.

The company confirmed the cost of Senza has not changed. Some published evidence and expert opinion have noted cases of proceeding straight to permanent implantation of Senza without an initial trial. However, the Senza instructions for use have not changed and refer to the use of a trial before permanent implantation. It is unlikely that an updated cost model would require a change to the recommendations

which state that the costs of Senza are similar to low frequency SCS devices over 15 years.

5. Evidence

5.1 New evidence

NICE information services identified 767 papers. The search date was limited from June 2017 to May 2022. Because of the new evidence volume, NICE commissioned an EAG for an evidence review. A total of 12 publications on 10 studies were included in the review (see details in section 4 of the EAG evidence review report).

The included studies had a sample size ranging from 11 (De Groote et al. 2020) to 113 (Peterson et al. 2021, Peterson et al. 2022a, Peterson et al. 2022b) people, including a range of patient subgroups:

- people with failed back surgery syndrome ((Kallewaard et al. 2021, De Groote et al. 2020, Abraham et al. 2021, Torres-Bayona et al. 2021)
- people with back pain (Kapural et al. 2022, Sayed et al. 2020, DiBenedetto et al. 2018)
- people with diabetic neuropathy (Chen et al. 2022, Peterson et al. 2022a, Peterson et al. 2022b, and Peterson et al. 2021)
- people with complex regional pain syndrome and failed back surgery syndrome (Cordero Tous et al. 2021)

The EAG noted that study populations included in studies were heterogeneous. For instance, there were differences in treatment history before using Senza. Key outcomes of the reviewed studies are summarised below:

- **Trial outcome**: a total of 7 studies reported on the proportion of people undergoing a successful trial ranging from 61% to 100%. The trial duration ranged between 5 days and 4 weeks, the definition of successful trial was diverse. Six studies defined trial success as more than 50% of pain reduction. The instructions for use for Senza only state that the device is contraindicated for those who have not had a successful trial, but do not explicitly state the

duration of trial period, nor define what is deemed as a successful trial outcome.

- **Pain scores and duration of pain relief**: a statistically significant reduction in back and leg pain scores were observed up to 12 months in 5 studies (Abraham et al. 2021, Sayed et al. 2020, Cordero Tous et al. 2021, DiBenedetto et al. 2018, and Peterson et al. 2022a and Peterson et al. 2022b reporting on the same study). Peterson et al. (2022b) also reported a statistically significant percentage reduction in pain at 6 and 12 months. Chen et al. (2022) reported pain outcomes at 24 months, with 88.9% (24/27) of patients still reporting at least 50% pain relief (n=27).

- **Patient satisfaction**: between 54% and 73% of people reported that their pain had improved “much” or “very much” at 12 months when compared with baseline (n=4 studies). Four studies reported that all people were satisfied with their treatment.

- **Health-related quality of life**: 4 single arm studies reported quality of life measures up to 12 months. However, the EAG cannot draw conclusions regarding efficacy because of the variability in tools used, at different follow-up time points, across different subgroups, and a lack of comparators. Peterson et al. (2022b) reported statistically significant improvements in components of the EQ-5D at 6 and 12 months when compared with baseline. Peterson et al. (2022b) also reported statistically significant improvements in all reported domains on the Diabetes Quality of Life instrument at 6 and 12 months.

- **Functional disability measures**: 5 single arm studies reported functional disability measures up to 12 months. However, the EAG cannot draw conclusions regarding efficacy because of the variability in tools used, at different follow-up time points, across different subgroups, and a lack of comparators.

- **Opioid and other analgesic use:** no comparative evidence reported on opioid use between Senza and conventional SCS. Between 7.0% and 71.4%

of people reported reduced use of opioids or analgesics (Kallewaard et al. 2021, DiBenedetto et al. 2018). Between 21.9% and 36.0% of people discontinued using opioids or analgesics (Kapural et al. 2022, Cordero Tous et al. 2021). Between 6.0% and 9.0% of people increased opioids or analgesics doses over the course of the study (Kapural et al. 2022, Cordero Tous et al. 2021). The EAG noted inconsistent, incomplete or likely incorrect reporting in Cordero Tous et al. (2021) and Kallewaard et al. (2021).

5.2 Device related events

Adverse events reported in the included studies were:

- implant site infection (Torres-Bayona et al. 2021, Kapural et al. 2022) Peterson et al. 2022a)
- implant site pain or discomfort (Kapural et al. 2022, Peterson et al.2021)
- neurologic deficits (Peterson et al. [2021, 2022b], Peterson et al. 2021, Kapural et al. 2022)
- other adverse events: transient cerebrospinal fluid leakage (Kapural et al. 2022); wound dehiscence (Peterson et al. 2021)

Senza was removed or reimplanted because of the following reasons:

- lead migration (Torres-Bayona et al. 2021, Kapural et al. 2022, Peterson et al. (2022b)
- infection (Torres-Bayona et al. 2021, Kapural et al. 2022)
- skin erosion at the implant site (Torres-Bayona et al. 2021)
- implant site pain (Kapural et al. 2022)

5.3 UK Neuromodulation Registry

The EAG was advised by the UK Neuromodulation Registry that there are an estimated [redacted] large implanting centres for SCS devices across the UK, along with some smaller centres implanting around 10 to 15 devices a year. Overall, around [redacted] enter their neuromodulation data into the registry.

The UK Neuromodulation Registry shared its data relating to Senza devices from [redacted] centers with the NICE review team. There are [redacted] Senza implants currently

registered, and [redacted] of these are in people relevant to the scope, with back or lower limb pain. There are currently [redacted] implants recorded with at least 12 months of follow up. The UK Neuromodulation Registry is intending to publish reports of the data, which will include all SCS devices, and will not identify specific manufacturers.

Analysis of data on Senza from the UK Neuromodulation showed that the majority of implants are in line with the indication.

[redacted]

It should be noted that data in the Neuromodulation Registry is incomplete as some centers do not enter data at all or enter partial data.

5.4 Results from NICE research commissioning

Not applicable. No research was commissioned.

5.5 Cost case

The company confirmed the cost of the technology has not changed since the original guidance. The EAG identified an economic study published by the Company following the original guidance (Taylor et al. 2020). This economic study used the exact same model structure and model parameters previously reviewed during the EAG Assessment Report (2019), however with added utility values and cost-effectiveness analysis. The study reported that 10 kHz spinal cord stimulation (SCS) would be cost-saving and cost-effective when compared with low-frequency non-rechargeable (mean savings, £7,170 [95% CI £6,767 to £7,573] per person) and rechargeable (mean savings, £3,352 [£3,313 to £3,792] per person) spinal cord stimulation devices.

The EAG noted that there is evidence of UK NHS centres no longer including a trial phase. This is likely to apply to both intervention and comparator arms and therefore the point estimates in both arms would reduce in the cost model. Because of the removal of the trial phase, the number of devices explanted (due to lack of reduction in pain) may increase in both Senza and conventional SCS arms, but impact of

removing the trial phase on clinical and economic outcomes is uncertain.The UK Neuromodulation Registry has limited data about trials of SCS devices. The registry includes a record of whether a trial had taken place but the data available may not be complete because completing the registry is not mandatory. Trial efficacy data is not collected. There are also delays in some centres between successful trial and permanent implants, with some waiting as long as 9 months. In some centres, they do not offer trial and move straight to permanent implantation. The EAG noted that trial efficacy was included in the economic model which led to guidance development. The EAG also noted that the economic model used to support guidance development was dependent upon the proportion of patients achieving optimal pain relief, and data on opioid usage is not recorded in the UK neuromodulation registry.

6 Summary of new information and implications for review

Company

The company noted 2 published studies (Petersen et al., 2022; Kapural et al., 2022). One study, a randomised controlled trial was submitted for nonsurgical refractory back pain (Kapural et al., 2022). The other study, also a randomised controlled trial was submitted for painful diabetic neuropathy (Petersen et al., 2022). Both studies were in the NICE information services searches.

The three experts that responded to the information request noted that there were new publications. In total, the experts identified 5 new studies since the publication of the guidance, including the 2 studies submitted by the company. The other 3 studies were excluded because they did not specifically use Senza (Amirdelfan et al., 2021; De Jaeger et al., 2021; Goudman et al., 2020).

Clinical experts

Three clinical experts responded to NICE's request for information. All 3 experts were familiar with the technology and had used it. One expert noted that Senza is used in most but not all implanting centres in the UK. Another expert said that it is used in secondary care. Experts said that in their local practice Senza is used for predominantly neuropathic low back and leg pain, with 1 expert clarifying in the setting of failed back surgery syndrome, painful diabetic neuropathy, complex

regional pain syndrome and persistent spinal pain syndrome type 1 and 2 (formerly known as failed back surgery syndrome). Experts also noted that these potential groups would specifically benefit from using Senza.

One expert was aware of different versions of this technology and another expert was aware of 2 different leads (percutaneous and surgical paddle). Two experts were aware of competing technologies, with 1 expert noting that there are several other companies that manufacture spinal cord devices for the same indications as Senza. Two experts agreed that training is needed, with 1 expert specifying that this should include both advanced pain and neuromodulation training. One expert noted that it is important for the staff to know how to programme the device. One expert noted that the national neuromodulation registry for all spinal cord stimulation devices was put in place to collect information on the usefulness and safety of these devices.

The experts have not identified any issues relating to the functioning, reliability and maintenance of this technology. There is no controversy about the technology and there have not been any significant changes to the clinical pathway. All experts said that the care pathway or evidence had not changed in a way that an update would result in a different recommendation.

MHRA and MAUDE search

D'Souza et al. (2022) found 1,651 reports submitted to the Manufacturer and User Facility Device Experience (MAUDE) between 01 January 2016 and 31 December 2020. These were specific to 'Nevro' and product code 'LGW'. The majority of entries were categorised as procedural complications (72.6%, n=1,198), followed by serious adverse events (10.5%, n=174), device-related complications (10.5%, n=173) and patient complaints (9.9%, n=164); with multiple categories being assigned in some cases. The EAG did an additional search and found further 946 MAUDE reports have been submitted between 01 January 2021 and 31 July 2022 when searching 'Nevro' and 'Senza'. These 936 reports included 666 injuries, 245 deaths, and 25 malfunctions. The EAG noted that these MAUDE reports were all related to the use of Nevro Senza device but not restricted to chronic neuropathic back and lower limb pain in line with the scope of this MTG41. The EAG also notes that the events

identified may not have been directly related to Senza, for example, a report may have been to MAUDE for a patient with a device implanted who subsequently died, but the device itself may not have been the cause of death

The EAG conducted a search of MHRA database on the 18 August 2022 using terms; “Nevro”, “Senza”, and identified one MHRA field safety notice issued on 30 April 2021, relating to incorrect MRI safety labelling (patients were given an incorrect implant/patient ID card that stated “MR conditional” when the device should have been identified as “MR unsafe”).

7 Implications for other guidance producing programmes

There is an option within the MTEP process to update the guidance within another piece of NICE guidance**.**

8 Implementation

The device is still available in the UK. One expert noted the device is used in GP practices but not widely used. The company stated in the submission that Senza SCS would expect to be used in about [redacted] hospitals in the UK, and it suggested that adoption of the technology varies by regions,

[redacted]

9 Equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others.

No equality issues were raised in the original guidance. People who likely benefit from this technology may have disabilities caused by issues with mobility if their condition has a substantial and long-term negative effect on their abilities to do normal daily activities. Disability is a protected characteristic under the Equality Act 2010.

Consultation paper sign off:

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Appendix 1 – explanation of options

If the published Medical Technologies Guidance needs updating NICE must select one of the options in the table below:

Options	**Consequences**	**Selected – 'Yes/No'**
Amend the guidance and consult on the review proposal	The guidance is amended but the factual changes proposed have no material effect on the recommendations.	No
Amend the guidance and do not consult on the review proposal	The guidance is amended but the factual changes proposed have no material effect on the recommendations.	No
Standard update of the guidance	A standard update of the Medical Technologies Guidance will be planned into NICE's work programme.	No
Update of the guidance within another piece of NICE guidance	The guidance is updated according to the processes and timetable of that programme.	No

If the published Medical Technologies Guidance does not need updating NICE must select one of the options in the table below:

Options	**Consequences**	**Selected – 'Yes/No'**
No change to the guidance	The guidance remains valid and is designated as static guidance. Literature searches are carried out every 5 years to check whether any of the Medical Technologies Guidance on the static list should be flagged for review.	Yes
Defer the decision to review the guidance	NICE will reconsider whether a review is necessary at the specified date.	No
Withdraw the guidance	The Medical Technologies Guidance is no longer valid and is withdrawn.	No

Appendix 2 – supporting information

Relevant Institute work

In progress

Neurostimulation of lumbar muscles for refractory non-specific chronic low back pain. NICE interventional procedures. Publication expected: September 2022

Percutaneous image-guided cryoablation of peripheral neuroma for chronic pain. NICE interventional procedures. Publication expected: TBC