NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Medical technology guidance

Assessment report overview

Senza Spinal Cord Stimulation (SCS) system for the treatment of chronic pain

This assessment report overview has been prepared by the Medical Technologies Evaluation Programme team to highlight the significant findings of the External Assessment Centre (EAC) report. It includes **brief** descriptions of the key features of the evidence base and the cost analysis, any additional analysis carried out, and additional information, uncertainties and key issues the Committee may wish to discuss. It should be read along with the company submission of evidence and with the EAC assessment report. The overview forms part of the information received by the Medical Technologies Advisory Committee when it develops its recommendations on the technology.

Key issues for consideration by the Committee are described in section 6, following the brief summaries of the clinical and cost evidence.

This report contains information that has been supplied as academic-in-confidence and has been redacted before publication. This overview also contains:

- Appendix A: Sources of evidence
- Appendix B: Comments from professional bodies
- Appendix C: Comments from patient organisations
- Appendix D: Claimed benefits and decision problem from scope
- Appendix E: Model parameters - costs and resource use

1 The technology

The Senza Spinal Cord Stimulation (SCS) System (Nevro Corp) is a neuromodulation technology that delivers electrical impulses to the spinal cord. The electrical impulses are delivered by small electrodes, which are placed via leads in the epidural space in the spinal cord near the region that supplies nerves to the painful area, and are connected to a compact, battery-powered neurostimulator implanted under the skin. The Senza SCS system, can be used to deliver low frequency SCS (2 Hz to 1,200 Hz) or a high frequency treatment (known as HF10 therapy). This novel treatment involves the delivery of high frequency (10 kHz), short duration (30 μsec), low-amplitude (1-5 mA) pulses to the T8-T11 spinal epidural space in a specific treatment algorithm. The Senza SCS system was CE marked as a class III device in May 2010.

2 Proposed use of the technology

2.1 Disease or condition

The Senza SCS system is intended for use in the management of chronic intractable pain of the trunk and/or limbs, including unilateral or bilateral pain associated with failed back surgery syndrome as well as intractable low back and leg pain.

Pain that persists for more than several months, or beyond the normal course of a disease or expected time of healing, is often defined as chronic. Chronic pain can affect people of all ages, although in general, its prevalence increases with age. Estimates of the prevalence of this condition in the UK vary from less than 10% to greater than 30% depending on the specific definition of chronic pain used. Chronic pain is accompanied by physiological and psychological changes such as sleep disturbances, irritability, medication dependence and frequent absence from work. Emotional withdrawal and depression are also common, which can strain family and social interactions.

2.2 Patient group

Back pain is common and has a significant impact. The prevalence of neuropathic pain has been reported between 8.2% and 8.9% (Fayaz et al. 2016). According to Hospital Episode Statistics (HES), an estimated 1,137 SCS implantations took place in England in 2015 (Hospital Episode Statistics 2014-15). Although this includes all indications for SCS, therefore SCS implantation for leg/back pain would be lower than the estimated figure.

2.3 Current management

NICE technology appraisal 159 on spinal cord stimulator implantation for chronic pain of neuropathic or ischaemic origin recommends SCS as a treatment option for adults with chronic pain of neuropathic origin who continue to experience chronic pain for at least 6 months despite appropriate conventional medical management, and who have had a successful trial of stimulation as part an appropriate multidisciplinary team assessment. Available devices for SCS deliver low frequency SCS and have either a rechargeable or a non-rechargeable battery. Conventional medical management involves a multidisciplinary approach and may include pharmacological interventions such as non-steroidal anti-inflammatory drugs, tricyclic antidepressants, anticonvulsants, analgesics and opioids as well as physiotherapy and psychological support. Spinal cord stimulation is not recommended as a treatment option for adults with chronic pain of ischaemic origin except in the context of research. This NICE Technology Appraisal guidance was last reviewed in February 2014 at which time newer devices such as Senza SCS were identified but no evidence was found which would change the recommendations.

NICE clinical guideline on neuropathic pain in adults: pharmacological management in non-specialist settings covers managing neuropathic pain (nerve pain) with pharmacological treatments (drugs) in adults in non-specialist settings. NICE guideline on low back pain and sciatica in over 16s:

assessment and management covers assessment of low back pain and sciatica and non-invasive and invasive treatment options.

2.4 Proposed management with new technology

If adopted Senza would be used as an alternative to traditional low-frequency SCS systems. Senza would be included in the same position in the pathway of care as traditional low-frequency (LF) SCS systems. It is therefore anticipated that little or no additional training or infrastructure requirements would be needed. Senza differs from other forms of SCS in not requiring paraesthesia mapping but other elements of the procedure are similar.

3 Company claimed benefits and the decision problem

These are described in the scope in Appendix D.

Table 1 Details of variation from the scope

Decision problem	Variation proposed by company	EAC view of the variation
Outcomes	The company omitted the following outcomes due to a lack of objective data from published trials; implantation time in theatre, follow up appointments, staff conducting device programming.	The EAC acknowledged this omission as reasonable.
Subgroups	The company omitted any subgroup analysis as the available clinical evidence indicated there was no significant difference in outcomes between previous back surgery / FBSS, chronic pain involving the limbs and chronic pain involving the back. In the case of complex regional pain syndrome there was no	The EAC acknowledged this omissions.

	comparative evidence available.	

The company correctly defined the population as patients undergoing spinal cord stimulation for chronic pain in line with NICE Technology Appraisal 159. However the EAC notes that the evidence from NICE Technology Appraisal 159 was restricted to patients with failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS) and that the company restricted their literature search to back and leg pain. Therefore the EAC concluded that for practical purposes, the population is restricted to patients with neuropathic pain of the lower back and legs.

4 The evidence

4.1 Summary of evidence of clinical benefit

The company carried out a literature search for published evidence. The EAC considered the eligibility criteria used by the company was generally consistent with the scope. The EAC re-ran the company's searches and did not find any additional relevant studies. Details of all the included and excluded studies are in table 2, a full description of the rationale can be found in section 3.3 of the assessment report.

Table 2 Included and excluded studies

Study	Type of publication	Type of study	Comment
Studies included by both EAC and company (n=6)			
6 studies included by both	*6 full papers*	*RCT* *Kapural et al. (2016)* *Comparative uncontrolled* *Tiede et al. (2013)* *Non-comparative observational studies* *Al-Kaisy et al. (2014)* *Russo et al. (2016)* *Rapcan et al. (2015)*	*The EAC deemed the Kapural et al. (2016) the pivotal study.*

		Al-Kaisy et al. (2017)	
Studies in submission excluded by EAC (n=1)			
De Caloris et al. (2017)	*Full paper*	*Non-comparative observational study*	*Excluded by EAC based on population and reported outcomes.*
Studies not in submission included by EAC (n=0)			
N/A	*N/A*	*N/A*	

EAC critical appraisal of the clinical evidence

The EAC reviewed the clinical evidence, and 6 of the 7 studies submitted were deemed relevant. Table 3.1 in the assessment report summarises the characteristics of each study.

The EAC conducted a critical appraisal of the evidence and concluded that the Kapural et al. (2016) RCT was the pivotal study because it reported relevant comparative data. The EAC identified the potential for performance, detection, and reporting bias in the SENZA-RCT and noted there was some inconsistency in the denominator used in the reporting of results. However, overall the EAC was satisfied that the trial's limitations and weaknesses were not of sufficient magnitude to affect the direction of results reported. The Al-Kaisy et al. (2014) was deemed the highest quality single arm study. The remaining 4 studies were limited by methodological quality or sample size, however the results complimented the findings of the 2 key studies and where appropriate relevant results are reported. Section 3.6 in the assessment report provides further details.

Results from the clinical evidence

Pain was predominantly reported using a VAS (visual analogue scale) score. In the SENZA-RCT, the VAS at 24 months was significantly lower compared with LF (low frequency) SCS for back (p=<0.001) and leg (p=<0.003) pain. In

the single-arm studies similar findings were reported (Al-Kaisy et al. 2014, Rapcan et al. 2015, and Russo et al. 2015).

The duration of pain relief was not an explicit outcome in any of the included studies, however 2 studies (Kapural et al. 2016 and Al-Kaisy et al. 2014) both reported improvements in pain relief at 24 months. The EAC concluded that there was sufficient evidence to suggest that Senza provides pain relief for a minimum of 24 months.

Five of the 6 studies included results on patient satisfaction, however reporting varied. In the comparative studies; more patients were very satisfied in the Senza group (60%) compared with the LF SCS group (40.4%) however this was not statistically significant (p=0.07) (Kapural et al. 2016): of patients who experienced both interventions, 88% preferred Senza (Tiede et al. 2013). In the single arm studies patients who were satisfied or very satisfied at 12 months ranged from 65-85% (Al-Kaisy et al. 2014 and Al-Kaisy et al. 2017). One study reported 81% of patients were satisfied or very satisfied at 24 months (Al-Kaisy et al. 2014).

Only 1 small (n=20) single arm study reported on health-related quality-of-life outcomes using data from SF-36 and EQ-5D questionnaires. The study showed statistically significant improvements across all time points (Al-Kaisy et al. (2017).

The most commonly used functional disability score used was the Oswestry Disability Index (ODI). The RCT showed a higher proportion of patients in the Senza group had minimal disability (23.5%) compared with the LF SCS group (9.9%) (Kapural et al. 2016). Three single arm studies all reported improvements in ODI scores. Other functional disability measures included the Patient Global Impression for Change (PGIC), the Clinician Global Impression for Change (CGIC) and the Global Assessment of Functioning (GAF), which all showed improvements. No data was reported on the ability to drive with Senza . Two single arm studies reported improvements in sleep.

Four studies reported some limited data on opioid and other analgesic use. In the RCT study, 35.5% of Senza patients decreased or eliminated opioid analgesic usage at 12 months compared with 26.4% of traditional SCS subjects (p= 0.41). In the single arm studies; 65% of patients had their opioid consumption reduced by a half at 12 months (Rapcan et al. 2015). 86% of patients were taking some form of opioid at baseline, which reduced to 57% at 24 months (p=< 0.001) (Al-Kaisy et al. 2014). Average daily opioid intake was reduced by 64% at 12 month (Al-Kaisy et al. 2017).

Device-related adverse events were reported in all of the included studies, however definitions of serious adverse events and adverse events varied (see section 3.7 in the assessment report for further details). The EAC concluded that Senza had a similar safety profile to LF SCS.

One study explicitly reported on the incidence of paraesthesia highlighting uncomfortable paraesthesia occurred in 0.0% of Senza subjects and 11.3% of LF SCS subjects (p= 0.001) (Kapural et al. 2016). Two single arm studies reported Senza was a paraesthesia free option (Rapcan et al. 2015 and Russo et al. 2016).

None of the included studies reported on implant lifetime. The maximum study follow up time is 24 months. Based on company information the Senza device with its rechargeable battery is expected to last for 10 years. Low frequency device lifetimes are dependent on whether rechargeable batteries are used.

The company provided unpublished academic in confidence data on reasons for implant removal based on the results of the SENZA-RCT. The data showed that after 2 years, [redacted] of patients implanted with a Senza device and [redacted] of patients with a LF SCS device had their device removed (further details on reasons for removal can be found in section 3.6.2 of the assessment report).

None of the studies reported on implantation time in theatre, the grade of staff conducting device programming and follow up appointments including attendance at pain clinics.

EAC conclusions on clinical evidence

The EAC concluded that there is good evidence from a RCT demonstrating Senza improves clinical outcomes compared with LF SCS for a minimum of 24 months (see tables 3.4 further details on patient outcomes). The single-arm studies although inferior in terms of methodological quality, generally supported the findings from the pivotal RCT. Table 3 highlights the EAC's view on the substantiation of the company's claimed benefits. The EAC also noted that there are no published studies comparing Senza with sham which is a limitation of the evidence base. There is also a lack of evidence for the use of Senza in conditions affecting the upper limbs, head, and neck.

Table 3 Substantiation of claimed patient benefits (taken from assessment report).

Claimed patient benefit (compared with low frequency SCS)	Substantiated?	EAC comment
Clinically superior pain relief (almost twice as much when measured using a VAS score) for the majority of patients with predominant back pain, as well as those with predominant leg pain.	Fully	Principal evidence from Senza-RCT supported by observational studies.
Increased achievement of a successful outcome (greater than or equal to a 50% reduction in pain) compared with low frequency SCS.	Fully	Evidence from Senza-RCT.
A significantly better functional outcome.	Fully	Substantiated by comparison of ODI scores and distribution.
The delivery of treatment without paraesthesia can therefore be continued during sleep and while driving or operating machinery.	Partially	Senza HF10 does not cause paraesthesia and driving is not contraindicated. Comparative sleep data not reported in published records of Senza-RCT.
Sustained and long term improvement in pain relief and function (RCT follow-up data currently to 24 months).	Fully	Comparative data supports efficacy up to 24 months.
May reduce the need for concomitant pain medication and potentially follow-up attendance at pain clinics.	Partially	Comparative evidence of opioid use (at 12 months) not conclusive. No data on follow up for pain clinics.
Abbreviation: ODI: Oswestry Disability Index.		

4.2 Summary of economic evidence

The company identified 1 study which met their inclusion criteria, a cost effectiveness study comparing Senza, to 4 other treatment options: conventional medical management (CMM) reoperation, and rechargeable and non-rechargeable low frequency (LF) SCS (Annemans et al., 2014).. The only difference between the rechargeable and non-rechargeable LF-SCS devices is the device longevity and the cost. The EAC conducted a literature search and identified the same study. The EAC considered the company's critical appraisal of the Annemans et al. (2014) study to be well conducted and agreed with their findings that the study was of a high quality. The study, which reproduced the original decision analytic model structure used to inform NICE technology appraisal guidance on spinal cord stimulator implantation for chronic pain of neuropathic or ischaemic origin (Simpson et al. 2008), concluded that Senza is cost-effective compared to CMM and reoperation, and dominant compared to both rechargeable and non-rechargeable LF SCS devices.

De novo analysis

The company presented a de novo economic model comparing Senza and additional CMM as required with non-rechargeable and rechargeable LF SCS. The population was adult patients experiencing chronic pain despite CMM in line with NICE technology appraisal guidance on spinal cord stimulator implantation for chronic pain of neuropathic or ischaemic origin. The company provided a model diagram of the 2 stage decision analytic model, which can be found in section 4.2.3 of the assessment report. The model, which was an iteration of the model previously developed to inform NICE technology appraisal guidance on spinal cord stimulator implantation for chronic pain of neuropathic or ischaemic origin (Simpson et al. 2008) has a decision tree for the first 6 months, followed by a Markov state transition model with a 15 year time horizon.

Model parameters

Most of the assumptions and parameters in the model were derived from the model used in NICE technology appraisal 159 and subsequently published. The clinical parameters were derived from the Senza-RCT (Kapural et al., 2015). For the base case the company used the clinical effectiveness parameters for leg pain. Some of the data such as the non-serious complications and explantation data from the Senza-RCT was made available by the company as academic-in-confidence. The EAC agreed with the parameters in the company's model and these are summarised in appendix E.

Model costs

In the model the costs associated with each clinical state were based on the degree of pain relief achieved and the presence of complications. There were also costs associated with the device trial, device implantation, explantation, device replacement, and reoperation. Most of the costs, were derived directly from the economic model used in the technology appraisal and since this model was dated February 2010, the company inflated the costs using inflation indices. The EAC judged that updating drug costs in this way is not appropriate and considers this a source of uncertainty within the model.

The Senza device cost used by the company in the base case was £16,648 which was based on the Annemans et al. (2016) study updated to 2016 prices. The cost is the system cost only and does not include implantation procedural costs. The company provided a list price as commercial in confidence. The company justified not using the list price in the base case as in reality the NHS would never pay the full list price. The comparator cost in the model was based on the Annemans et al. (2016) study updated to 2016 prices. A key driver of costs in the model was device longevity, with an assumed useful battery duration of 4 year (range 2 to 6 years) for non-rechargeable implants and 10 years (range 9 to 25 years) for rechargeable technologies.

Results

Table 4 outlines the company's overall base case results. Over a 15 year time horizon Senza saved £4,795 per patient compared with rechargeable LF SCS, this amounted to an annual saving of £320 per patient. Compared with non-rechargeable LF SCS, Senza saved £7,755 over 15 years per patient, this equated to an annual saving of £517 per patient.

Table 4 Company base case results over 15 years

Device	Comparator	Difference over 15 years
Senza and CMM	Non-rechargeable LF SCS and CMM	£7,755
Senza and CMM	Rechargeable LF SCS and CMM	£4,795

The EAC considered the company's de novo model as being of high methodological quality, with appropriate and comprehensive reporting of results and sensitivity analysis. It agreed with the company's basecase results. A breakdown of the comparative costs at different stages of the patient pathway showed that Senza generated most of its savings because of reduced pain management and complication costs after the first 6 months. Further details are in table 4.5 of the assessment report. The EAC understands from clinical experts that, in the UK, most implants are non-rechargeable (NYEAC, 2017).

Sensitivity analysis

The company provided a comprehensive univariate sensitivity analysis as part of their submission. In the majority of cases Senza was cost saving compared with the comparators. In instances where Senza was cost incurring the EAC considered most of these scenarios to be not plausible. Further details can be found in table 4.6 of the assessment report. The main cost drivers were drug pain therapy and device longevity.

Parameters that were identified as sensitive to univariate analysis were further scrutinised using threshold analysis by the company. There was uncertainty

around the costs of implantation (device and procedural costs) and device longevity. The threshold analysis showed that Senza was cost neutral at an implant price of £21,000 and device longevity of 7 years. Equally rechargeable LF SCS would become cost saving compared to Senza if the implantation cost fell below £13,500 or if the device remained in situ for 15 years.

Probabilistic sensitivity analyses carried out by the company showed that Senza was cost saving in 73% and 74% compared to rechargeable and non-rechargeable LF SCS respectively.

EAC conclusions on the economic evidence

The EAC concluded the company's *de novo* model was of a high methodological standard and reasonably robust. It considered that strengths of the model include its basis on a structure and inputs which have already been scrutinised and accepted by experts and its consistent use of conservative assumptions which have been verified as such by clinical experts. The model also employed deterministic and probabilistic sensitivity analyses to test these assumptions and uncertainties. The model has some weaknesses or limitations, which are unavoidable when the clinical evidence base is not complete. Some of the model parameters are based on small sample sizes and the uncertainty is compounded by extrapolation of data required by the 15 year time horizon of the model.

The EAC considers that the basecase saving are relatively modest (approximately £320 and £500 per annum, accounting for 5% and 8% of total costs) but are probably conservative, and do not take into account increased patient benefit. It considered the extensive sensitivity analyses, including PSA did not change the direction of the cost savings except in implausible scenarios. The EAC concluded that Senza is cost saving compared with LF

SCS therapy, in the population indicated by TA159, and that its introduction into the NHS should release healthcare resources.

5 Ongoing research

In total 12 ongoing or terminated studies were identified by the company and/or the EAC. Further details of these studies can be found in section 3.8 and appendix C of the assessment report.

6 Issues for consideration by the Committee

Clinical evidence

- The population specified in the scope is "patients undergoing spinal cord stimulation for chronic pain in line with NICE Technology Appraisal 159." The evidence from NICE Technology Appraisal 159 was restricted to patients with failed back surgery syndrome (FBSS) and complex regional pain syndrome (CRPS), and the EAC concluded that there is a lack of evidence for the use of Senza in conditions affecting the upper limbs and head. Additionally, the company restricted their literature search to back and leg pain. The pivotal SENZA-RCT had a population which included 77% of patients with FBSS. Therefore should any recommendations be based on patients solely with neuropathic pain of the lower back and/or legs who have had FBSS?
- NICE Technology Appraisal 159 assumed all low frequency SCS devices equivalent in terms of effectiveness. Should the same approach be taken in this evaluation?

Cost evidence

- The EAC considered that a weakness of the model was that it included only device costs and did not consider any differences in implantation procedure costs such as consultation, investigations, surgery and hospital admissions,

which were included in TA 159 (Simpson *et al.*, 2008). Is this a reasonable assumption?

- Pain management costs were a key driver in the model. These costs were based on inflated 2016 values. The cost of drugs may have changed because of the introduction of generic compounds or increased use of proton pump inhibitors (in combination with NSAIDs) or changes in clinical practice. In a similar way non-drug costs may also have changed because of changes to clinical pathways and practice since TA 159 was first authored. Is this a reasonable assumption?
-

7 Authors

Liesl Millar, Technical Analyst

Bernice Dillon, Technical Adviser

NICE Medical Technologies Evaluation Programme

September, 2017

Appendix A: Sources of evidence considered in the preparation of the overview

A Details of assessment report:

- Willits, I. et al. Senza Spinal Cord Stimulation (SCS) System for the treatment of chronic pain, (August 2017)

B Submissions from the following sponsors:

- Nevro Corporation

C Related NICE guidance

- Spinal cord stimulator implantation for chronic pain of neuropathic or ischaemic origin. NICE technology appraisal guidance 159 (2008). Available from www.nice.org.uk/guidance/TA159
- Neuropathic pain in adults: pharmacological management in non-specialist settings. NICE clinical guideline 173 (2017). Available from https://www.nice.org.uk/guidance/cg173
- Low back pain and sciatica in over 16s: assessment and management. NICE guideline 59 (2016). Available from https://www.nice.org.uk/guidance/ng59
-

D References

Al-Kaisy A, Palmisani S, Smith T E, Pang D, Lam K, Burgoyne W, Houghton R, Hudson E and Lucas J 2017 10 kHz High-Frequency Spinal Cord Stimulation for Chronic Axial Low Back Pain in Patients With No History of Spinal Surgery: A Preliminary, Prospective, Open Label and Proof-of-Concept Study Neuromodulation 20 63-70

Al-Kaisy A, Van Buyten J P, Smet I, Palmisani S, Pang D and Smith T 2014 Sustained effectiveness of 10 kHz high-frequency spinal cord stimulation for patients with chronic, low back pain: 24-month results of a prospective multicenter study Pain medicine (Malden, Mass.) 15 347-54

Annemans L, Van Buyten J P, Smith T and Al-Kaisy A 2014 Cost effectiveness of a novel 10 kHz high-frequency spinal cord stimulation system in patients with failed back surgery syndrome (FBSS) Journal of long-term effects of medical implants 24 173-83

De Carolis G, Paroli M, Tollapi L, Doust M W, Burgher A H, Yu C, Yang T, Morgan D M, Amirdelfan K, Kapural L, Sitzman B T, Bundschu R, Vallejo R, Benyamin R M, Yearwood T L, Gliner B E, Powell A and Bradley K 2017 Paresthesia-Independence: An Assessment of Technical Factors Related to 10 kHz Paresthesia-Free Spinal Cord Stimulation Pain Physician 20 331-41

Hospital Episode Statistics 2014-15. Admitted Patient Care. Procedures and Interventions. http://content.digital.nhs.uk/searchcatalogue?productid=19420&q=title%3a%22Hospital+Episode+Statistics%2c+Admitted+patient+care+-+England%22&sort=Relevance&size=10&page=1#top

Kapural L, Yu C, Doust M, Gliner B, Vallejo R, Sitzman B T, Amirdelfan K, Morgan D, Brown L, Yearwood T, Bundschu R, Burton A, Yang T, Benyamin R and Burgher A 2016a Sustained pain relief and quality of life improvement in chronic back pain subjects treated with 10 kHz high frequency spinal cord stimulation (SCS): Results from a randomized controlled trial (SENZA-RCT). In: Regional anesthesia and pain medicine.

Kapural L, Yu C, Doust M W, Gliner B E, Vallejo R, Sitzman B T, Amirdelfan K, Morgan D M, Brown L, Yearwood T L, Bundschu R, Burton A W, Yang T, Benyamin R and Burgher A H 2015 Novel 10-kHz High-frequency Therapy (HF10 Therapy) Is Superior to Traditional Low-frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: The SENZA-RCT Randomized Controlled Trial Anesthesiology 123 851-60

Kapural L, Yu C, Doust M W, Gliner B E, Vallejo R, Sitzman B T, Amirdelfan K, Morgan D M, Yearwood T L, Bundschu R, Yang T, Benyamin R and Burgher A H 2016c Comparison of 10-kHz High-Frequency and Traditional Low-Frequency Spinal Cord Stimulation for the Treatment of Chronic Back and Leg Pain: 24-Month Results From a Multicenter, Randomized, Controlled Pivotal Trial Neurosurgery 79 667-77

Kumar K, Taylor R S, Jacques L, Eldabe S, Meglio M, Molet J, Thomson S, O'Callaghan J, Eisenberg E, Milbouw G, Buchser E, Fortini G, Richardson J and North R B 2007 Spinal cord stimulation versus conventional medical management for neuropathic pain: a multicentre randomised controlled trial in patients with failed back surgery syndrome Pain 132 179-88

NICE 2008 Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin (TA159). (London: National Institute for Health and Care Excellence)

NICE 2013 Review of TA159; Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin. (London: National Institute for Health and Care Excellence)

NICE 2016 Low back pain and sciatica in over 16s: assessment and management (NG59). (London: National Institute for Clinical Excellence)

NICE 2017a Neuropathic pain –pharmacological management: The pharmacological management of neuropathic pain in adults in non-specialist settings (CG173). (London: National Institute for Health and Care Excellence)

North R B, Kidd D H, Farrokhi F and Piantadosi S A 2005 Spinal cord stimulation versus repeated lumbosacral spine surgery for chronic pain: a randomized, controlled trial Neurosurgery 56 98-106; discussion -7

Rapcan R, Mlaka J, Venglarcik M, Vinklerova V, Gajdos M and Illes R 2015 High-frequency - Spinal Cord Stimulation Bratisl Lek Listy 116 354-6

Russo M, Verrills P, Mitchell B, Salmon J, Barnard A and Santarelli D 2016 High Frequency Spinal Cord Stimulation at 10 kHz for the Treatment of Chronic Pain: 6-Month Australian Clinical Experience Pain Physician 19 267-80

Simpson E L, Duenas A, Holmes M W and Papaioannou D 2008 Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin (Technology Assessment Report). (The University of Sheffield,: School of Health and Related Research (ScHARR))

Taylor R S, Ryan J, O'Donnell R, Eldabe S, Kumar K and North R B 2010 The cost-effectiveness of spinal cord stimulation in the treatment of failed back surgery syndrome The Clinical journal of pain 26 463-9

Tiede J, Brown L, Gekht G, Vallejo R, Yearwood T and Morgan D 2013 Novel spinal cord stimulation parameters in patients with predominant back pain Neuromodulation 16 370-5

Appendix B: Comments from professional bodies

Expert advice was sought from experts who have been nominated or ratified by their Specialist Society, Royal College or Professional Body. The advice received is their individual opinion and does not represent the view of the society.

Dr Rajiv Chawla

Consultant in Pain Medicine and Neuromodulation, British Pain Society

Diarmuid Denneny

Physiotherapy Lead, Chartered Society of Physiotherapy

Professor Paul Eldridge

Consultant Neurosurgeon, Professor of Neurosurgery, Royal College of Surgeons; Society British Neurological Surgeons, British Pain Society

Dr Bernhard Frank

Consultant in Pain Medicine, International Association for the Study of Pain (IASP), Neuropathic Pain Specialist Interest Group at the IASP, British Pain Society, Royal College of Anaesthetists, British Medical Association

Mr Alistair Jenkins

Consultant Neurosurgeon, Society of British Neurological Surgeons

Dr Sarah Love-Jones

Pain Consultant, British Pain Society

Ms Karen Sanderson

Advanced Nurse Practitioner, Royal College of Nursing

Manohar Sharma

Consultant in Pain Medicine, British Pain Society, Royal College of Anaesthetists

Dr Tim Johnson

Consultant in Pain Management, British Pain Society

Mr Girish Vajamani

Consultant Neurosurgeon, Society of British Neurological Surgeons

All 10 specialist commentators were familiar with or had used this technology before. Two of the commentators were involved in clinical trials of the device.

Level of innovation

The majority of the specialist commentators considered the Senza SCS system to be a significant variation on current clinical practice with a novel design and concept. One noted that this technology is the first to provide paraesthesia- free stimulation. Some of the commentators noted that the hardware is similar to low frequency SCS, however the delivery of the SCS is different.

Potential patient impact

Seven of the specialist commentators stated that this technology could be of particular benefit to patients with failed back surgery syndrome; however one felt that more evidence might be needed to compare the device against a placebo. Three thought that this would be useful for patients with neuropathic back pain. Patients with complex regional pain syndrome (CRPS) may also benefit from this technology.

A key impact of this technology noted by the commentators is the avoidance of paraesthesia (tingling sensation) found in low frequency stimulation. Four commentators felt that this could be particularly beneficial for people unable to tolerate paraesthesia or for those who need to drive. Another noted that using Senza SCS changes the patient experience as no paraesthesia is felt and by the avoidance of postural changes in therapy. Four commentators noted that this avoids the need for on-table patient testing (paraesthesia mapping), which also makes the procedure quicker. One specialist commentator stated using the Senza SCS system reduced the number of visits to specialist units as less reprogramming is required.

Potential system impact

One commentator noted that spinal cord stimulation is already recommended by NICE, therefore implementation would be relatively barrier-free as centres already providing this type of treatment would be able to adopt the Senza SCS system using their existing facilities. Three felt that due to the shorter theatre time, more patients could be treated with the Senza SCS system. Three specialist commentator also stated that using this technology requires less follow up appointments compared to conventional SCS. Five commentators stated that training needed to use this device would be similar to that of low frequency stimulation.

Appendix C: Comments from patient organisations

Advice and information was sought from patient and carer organisations. The following patient and carer organisations responded:

- British Pain Society*

The following patient organisations were contacted and no response was received.

- Back Care
- British Orthopaedic Association - Patient Liaison group
- Fighting Back UK
- Action on Pain
- Pain Association Scotland
- Pain Concern
- Pain Relief Foundation
- Pain UK

*Comments on the Senza SCS were invited from the British Pain Society which, in place of providing a patient commentary, suggested Dr Tim Johnson as a Specialist Commentator.

Appendix D: Claimed benefits and decision problem from scope

The benefits to patients claimed by the company compared with low frequency SCS are:

- Clinically superior pain relief (almost twice as much when measured using a VAS score) for the majority of patients with predominant back pain, as well as those with predominant leg pain.
- Increased achievement of a successful outcome (greater than or equal to a 50% reduction in pain) compared with low frequency SCS.
- A significantly better functional outcome.
- The delivery of treatment without paraesthesia can therefore be continued during sleep and while driving or operating machinery.
- Sustained and long term improvement in pain relief and function (RCT follow-up data currently to 24 months).
- May reduced the need for concomitant pain medication and potentially follow-up attendance at pain clinics.

The benefits to the healthcare system compared with low frequency SCS claimed by the sponsor are:

- Avoidance of the need for paraesthesia mapping facilitating shorter and more predictable implantation procedural times
- May reduce the need for concomitant pain medication and potentially follow-up attendance at pain clinics.

	Scope issued by NICE
Population	Patients undergoing spinal cord stimulation for chronic pain in line with NICE Technology Appraisal 159
Intervention	HF10 therapy using the Senza spinal cord simulation system
Comparator(s)	Low frequency spinal cord stimulation (up to 1200 Hz)
Outcomes	The outcome measures to consider include: • Pain scores (for example VAS score) • Duration of pain relief • Patient satisfaction relating for example to frequency of battery recharging. • Health-related quality-of-life • Functional disability measures e.g. disability Index Score, Oswestry Disability Index and functional improvement including ability to drive and perform work-related activities • Opioid and other analgesic use • Device-related adverse events • Implantation time in theatre • Incidence of paraesthesia • Implant lifetime • Reason for implant removal • Follow up appointments including attendance at pain clinics • Staff conducting device programming

Appendix E: Model parameters - costs and resource use

Clinical data variables in the decision tree (6-months)		
Model parameter	**Base case (95% CI)**	**Source**
Trial success		
HF10™ therapy	92.8% (87.6%-97.9%)	Kapural et al. (2015)
TR-SCS/TNR-SCS	88.0% (81.4%-94.7%)	Kapural et al. (2015)
Optimal pain relief (leg pain, 6 months)		
HF10™ therapy	80.9% (72.7%-89.1%)	Kapural et al. (2015)
TR-SCS/TNR-SCS	54.4% (43.5%-65.2%)	Kapural et al. (2015)
CMM alone	9.3% (8.4%-10.2%)	Taylor et al. (2010)
Non-serious complications (6 months)		
HF10™ therapy	[redacted]	SENZA-RCT, data on file
TR-SCS/TNR-SCS	[redacted]	SENZA-RCT, data on file
Calculated values from the SENZA-RCT		
Optimal pain relief without complications		
HF10™ therapy	[redacted]	Calc from SENZA-RCT
TR-SCS/TNR-SCS	[redacted]	Calc from SENZA-RCT
Optimal pain relief with complications		
HF10™ therapy	[redacted]	Calc from SENZA-RCT
TR-SCS/TNR-SCS	[redacted]	Calc from SENZA-RCT
Sub-optimal pain relief without complications		
HF10™ therapy	[redacted]	Calc from SENZA-RCT
TR-SCS/TNR-SCS	[redacted]	Calc from SENZA-RCT
Sub-optimal pain relief with complications		
HF10™ therapy	[redacted]	Calc from SENZA-RCT
TR-SCS/TNR-SCS	[redacted]	Calc from SENZA-RCT
Clinical data variables in the Markov model		
Model parameter	**Base case (95% CI)**	**Source**
Non-serious complications (beyond 6 months)		
HF10™ therapy	[redacted]	SENZA-RCT, data on file
TNR-SCS/TR-SCS	[redacted]	SENZA-RCT, data on file
Explant rate (Year 1)		
HF10™ therapy	[redacted]	SENZA-RCT, data on file
TNR-SCS/TR-SCS	[redacted]	SENZA-RCT, data on file
Explant rate (Year 2)		
HF10™ therapy	[redacted]	SENZA-RCT, data on file
TNR-SCS/TR-SCS	[redacted]	SENZA-RCT, data on file
Explant rate (Year 3 and beyond)		
HF10™ therapy	3.2% (0%-15.8%)	Simpson et al. (2009)
TNR-SCS/TR-SCS	3.2% (0%-15.8%)	Simpson et al. (2009)
Other clinical data variables in the Markov model		
Model parameter	**Base case (95% CI)**	**Source**
Annual death rate	0.8% (0.7%-0.9%)	ONS (England)
No. of patients receiving a reoperation per annum	5.0% (4.5%-5.5%)	Simpson et al. (2009)
No. of patients achieving optimal pain relief post-surgery after reoperation	19.0% (17.1%-20.9%)	Simpson et al. (2009)