NICE advice

# Evoke Spinal Cord Stimulator for managing chronic neuropathic or ischaemic pain

Medtech innovation briefing
Published: 8 December 2020

www.nice.org.uk/guidance/mib238

## Summary


- The **technology** described in this briefing is Evoke Spinal Cord Stimulator System. It is used for managing chronic neuropathic or ischaemic pain.
- The **innovative aspects** are that Evoke uses a 'closed-loop' feedback control. It does this by recording activation of neural tissue and automatically adjusting stimulation to ensure it remains in the therapeutic range.
- The intended **place in therapy** would be as a replacement or alternative to current open-loop (fixed-output) spinal cord stimulation therapy in people with leg and back pain.
- The **main points from the evidence** summarised in this briefing are from 2 studies: a randomised controlled trial and an observational study, including a total of 184 adults with intractable back and leg pain. They show that Evoke is more effective than open-loop spinal cord stimulation in people with intractable back and leg pain.

- **Key uncertainties** around the evidence are that there are no studies reporting the economic impact of Evoke.
- The **cost** of Evoke ranges from £17,595 to £19,395 for the device. The trial phase cost ranges from £1,920 to £4,975. The **resource impact** would be comparable with standard care, which ranges from £13,726 to £22,418 for a rechargeable spinal cord stimulation system.

# The technology

The Evoke system (Saluda Medical) is a rechargeable, implantable, closed-loop stimulator for chronic pain management. The system is made up of an implantable closed-loop stimulator (an external stimulator is used during an initial trial period), 1 or 2 12-contact leads connecting the stimulator to the spinal cord, a remote control for manually changing stimulation and a charging kit. The stimulator (external or implantable) is programmed to deliver therapeutic spinal cord stimulation using feedback control with the Evoke Clinical Interface and Evoke Clinical System Transceiver. Evoke can be programmed and used as an open-loop (which gives a fixed output of stimulation) spinal cord stimulation system, similar to conventional spinal cord stimulation systems.

## Innovations

Evoke uses feedback control by recording activation of neural tissue and automatically adjusting spinal cord stimulation to ensure it remains in the therapeutic range. The company claims using Evoke could improve pain management and reduce follow-up appointments.

## Current care pathway

Treatment for chronic pain is to make pain tolerable and improve people's functionality and quality of life. In cases when the cause of the pain cannot be treated, pain pathways are adjusted to manage the pain severity. People presenting with chronic pain will be assessed by a multidisciplinary team experienced in managing chronic pain. Treatment is based on the presentation and severity of the pain and includes pharmacological and non-pharmacological interventions. Pharmacological interventions include non-steroidal anti-inflammatory drugs, tricyclic antidepressants, anticonvulsants, analgesics and opioids. Non-pharmacological interventions include physiotherapy, psychological therapy and

spinal cord stimulation. Spinal cord stimulation is recommended for people who have neuropathic pain and have had a successful spinal cord stimulation trial.

The following publications have been identified as relevant to this care pathway:

- NICE's guideline on neuropathic pain in adults: pharmacological management in non-specialist settings
- NICE's technology appraisal guidance on spinal cord stimulation for chronic pain of neuropathic or ischaemic origin
- NICE's medical technologies guidance on Senza spinal cord stimulation system for delivering HF10 therapy to treat chronic neuropathic pain
- NICE's guideline on low back pain and sciatica in over 16s: assessment and management.

# Population, setting and intended user

Evoke is intended as a replacement or alternative to the current open-loop spinal cord stimulation systems used in standard care to treat chronic, intractable pain. Deciding to implant the permanent Evoke closed-loop stimulator would depend on the successful completion of a trial period using the Evoke external closed-loop stimulator.

Treatment would be managed by a multidisciplinary team with experience in neuromodulation. The Evoke system would be implanted by specialist pain consultants or surgeons in an operating theatre. Programming is carried out by specialist pain nurses or specialist pain consultants. Follow-up procedures can take place on wards or in outpatient departments.

# Costs

## Technology costs

Evoke costs include the cost of the permanent device with either 1 or 2 leads.

- Evoke with 1 lead costs £17,595 (including electrodes, leads, implantable pulse generator, remote control, and battery charger).

- Evoke with 2 leads costs £19,395 (including electrodes, leads, implantable pulse generator, remote control, and battery charger).

The cost does not include the trial phase. The trial phase cost ranges from £1,920 to £4,975.

### Costs of standard care

NICE's technology appraisal guidance on spinal cord stimulation for chronic pain of neuropathic or ischaemic origin describes spinal cord stimulation devices (including stimulator, controller and charger, but excluding leads) as ranging from £6,858 to £13,289. The cost of leads ranges from £928 to £1,804 for surgical implantation and £1,065 to £1,158 for percutaneous implantation. However, these costs were last reviewed in 2013. NICE's medical technologies guidance on Senza spinal cord stimulation system for delivering HF10 therapy to treat chronic neuropathic pain reports more recent costs:

- Senza costs £16,648 (including electrodes, leads, implantable pulse generator, remote control, and battery charger).
- Non-rechargeable spinal cord stimulation system costs £11,281 (from £8,888 to £14,516), with a lifespan of 4 years.
- Rechargeable spinal cord stimulation system costs £17,422 (from £13,726 to £22,418).

An updated version of the Senza spinal cord stimulation system is now available, called Senza Omnia (2500). Costs may be higher than those listed above. Experts noted that the device costs listed here may have changed since the time of the NICE publication.

## Resource consequences

The device has been launched in the UK and is currently being used in 5 trusts.

Evoke would be used as a replacement option for current open-loop spinal cord stimulation devices in the NHS and the care pathway would remain unchanged. The costs for Evoke are in the range of conventional open-loop spinal cord stimulation systems currently available in the NHS.

# Regulatory information

Evoke is a CE-marked class 3 medical device.

# Equality considerations

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 identified in the development of this briefing.

# Clinical and technical evidence

A literature search was carried out for this briefing in accordance with NICE's interim process and methods statement. This briefing includes the most relevant or best available published evidence relating to the clinical effectiveness of the technology. Further information about how the evidence for this briefing was selected is available on request by contacting mibs@nice.org.uk.

## Published evidence

There are 2 studies summarised in this briefing. These include a randomised controlled trial (Mekhail et al. 2020) of 134 people and an observational study (Russo et al. 2020) of 50 people.

The clinical evidence and its strengths and limitations is summarised in the overall assessment of the evidence.

## Overall assessment of the evidence

The evidence base is small but includes comparative evidence of good methodological quality. The population and clinical outcome of pain rating are relevant to the NHS. The studies also reported system-related secondary outcomes including use of pain medication and number of follow-up visits related to reprogramming. Neither study included in the evidence base compares Evoke with a spinal cord stimulation device

routinely used in the NHS. Evidence showing equivalence between the open-loop Evoke used in the randomised controlled trial and open-loop spinal cord stimulation devices used as standard care would be useful. However, experts have stated the device is likely to be comparable. Both studies were funded by the company.

## Mekhail et al. (2020)

### Study size, design and location

Randomised controlled trial of 134 patients with chronic and intractable back and leg pain comparing the safety and efficacy of the closed-loop Evoke system with conventional open-loop spinal cord stimulation using Evoke in the US.

### Intervention and comparator

The intervention arm of the trial used closed-loop spinal cord stimulation. The comparator arm of the trial used fixed-output, open-loop spinal cord stimulation. Both the intervention and comparator devices use the same device (that is, Evoke).

### Key outcomes

The primary outcome was to achieve 50% or greater reductions in back and leg pain without an increase in pain medication. Out of the 125 people included in the study at 3 months, more people in the closed-loop group had a 50% or more reduction in pain compared with the open-loop group (82% and 60%, respectively). This shows statistically significant non-inferiority ($p<0.0001$) and superiority ($p<0.005$). Similarly, of the 118 people included in the study at 12 months, 83.1% of people in the closed-loop group had a 50% or more reduction in pain compared with 61.0% of people in the open-loop group (non-inferiority, $p<0.0001$; superiority, $p=0.006$). At 12 months, opioid use was reduced or eliminated in 55% of people in the closed-loop group and 40% of the open-loop group.

### Strengths and limitations

This was a well-designed double-blinded study with a computerised randomisation sequence for group allocation. Patient demographics were well matched between groups. The study was powered to detect non-inferiority and superiority between the 2 groups. The same device was used in both arms but only the interventional arm used the closed-loop system. The open-loop Evoke system has not been proven to be equivalent to

commercially available open-loop spinal cord stimulation devices, but experts advised it is likely to be comparable. The study was funded by the company and done outside of the UK.

## Russo et al. (2020)

### Study size, design and location

Open label, single arm prospective observational study of 50 people who were given the Evoke closed-loop spinal cord stimulation system to treat lower back or leg pain in Australia.

### Intervention and comparator

Evoke closed-loop system.

No comparator.

### Key outcomes

After 12 months, a reduction of 50% or more from baseline in pain rating was reported by 76.9% and 79.3% of people with back pain and people with leg pain, respectively. A reduction of 80% or more from baseline was reported in 56.4% and 58.6% of people with back and leg pain, respectively. At 12 months, mean overall pain reduced from a baseline of 81.3 mm on the visual analogue scale (plus or minus 1.6 mm) to 21.0 mm (plus or minus 3.4 mm, $p<0.001$). The proportion of people who reported 50% or more reduction from baseline in overall pain rating was 81.4%. There were 53.5% of people who reported 80% or more reduction in overall pain rating. The stimulation was in the therapeutic window 84.9% of the time and opioid intake was reduced or eliminated by the 12-month visit in 68.8% of people. The mean number of unscheduled programming visits per person was 2.41 (n=49) between month 0 and 1 and reduced to 0.14 between months 6 and 12 (n=43).

### Strengths and limitations

The study is multicentred and reported using Evoke in a relevant patient population. Clinical outcome measures were relevant and follow-up time was reasonable. The lack of comparator limits the usefulness of the findings. The study was powered to show that 90% of people could have programming with closed-loop stimulation. The study may be

underpowered to detect a difference from baseline in pain ratings. It was funded by the company and the primary author has previously served as a consultant to the company. The study was done outside of the UK.

## Sustainability

The company has not submitted any sustainability claims.

## Recent and ongoing studies

- Safety and efficacy study of the Evoke spinal cord stimulation system with feedback versus conventional stimulation (EVOKE). Trial identifier: NCT02924129. Status: active, not recruiting. Estimated completion date: June 2021, interim results published.
- A feasibility study of Evoke spinal cord stimulator system in subjects with chronic pain of the upper limb and/or neck. Trial identifier: ACTRN12618001808235. Status: recruiting.
- A prospective, feasibility study evaluating the safety and effectiveness of Saluda Medical's neurostimulation technology incorporating neural response measurement and feedback control to treat patients with chronic pain in an extended trial. Trial identifier: ACTRN12614000684628. Status: recruitment completed (last update 5 October 2018). Location: Australia.

# Expert comments

Comments on this technology were invited from clinical experts working in the field and relevant patient organisations. The comments received are individual opinions and do not represent NICE's view.

Three experts were involved in the development of this briefing. Two have used the device and all 3 were familiar with the technology.

## Level of innovation

All of the experts said that Evoke is the first spinal cord stimulation device to record neurophysiological data and adjust the therapeutic stimulation in response. Two experts

said the recording of physiological data would add valuable information. One expert said that other technologies have been designed to compensate for differences in stimulation because of changes in position by using sensors, but they do not use neurophysiological data.

## Potential patient impact

Experts identified sustained pain relief and quality of life as the main patient benefits. One expert said the device could reduce the likelihood of long-term failure of spinal cord stimulation treatment. Another said that it might reduce the number of people who become tolerant to spinal cord stimulation treatment. Experts identified that this device might be particularly beneficial to people who have difficulty detecting or describing the tingling sensation used for subjective feedback of spinal cord stimulation devices, or people who want to continue driving or maintain a physically demanding job.

## Potential system impact

Experts said that Evoke could reduce hospital follow-up visits because of improved pain management over time. One said that using Evoke could also reduce the use of pain management medication. One said that using objective neurophysiological data will reduce the reliance of clinicians on subjective feedback from patients. All experts expect Evoke to cost about the same as standard care.

## General comments

Experts said there might be a learning curve related to programming the closed-loop spinal cord stimulation system. Evoke will become another option that can be considered for people with chronic pain, it is likely to replace traditional implants used in the NHS. Evoke has only been used in a small number of patients across the UK. Experts said the slow uptake may be related to the COVID-19 pandemic, but they do not consider there to be any barriers to adoption.

# Expert commentators

The following clinicians contributed to this briefing:

- Dr Ganesan Baranidharan, consultant in anaesthesia and pain medicine, Leeds Teaching Hospitals NHS Foundation Trust. Did not declare any interests.
- Dr Bernhard Frank, consultant in pain medicine and honorary senior clinical lecturer in pain medicine, The Walton Centre NHS Foundation Trust. Did not declare any interests.
- Dr Ashish Gulve, consultant in pain management, department of pain medicine, The James Cook University Hospital. Dr Gulve has received financial support from the company for attending medical conferences and conference accommodation.

# Development of this briefing

This briefing was developed by NICE. NICE's interim process and methods statement sets out the process NICE uses to select topics, and how the briefings are developed, quality-assured and approved for publication.

ISBN: 978-1-4731-3934-3