NICE National Institute for Health and Care Excellence

NICE guidance

Axonics sacral neuromodulation system for treating refractory overactive bladder

Medical technologies guidance
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Contents

This guidance replaces MIB164.

1 Recommendations

1.1 Evidence supports the case for adopting Axonics sacral neuromodulation (SNM) system for treating refractory overactive bladder in the NHS. Axonics SNM system improves symptoms and quality of life. It also has a longer battery life than the non-rechargeable system used in NHS clinical practice.

1.2 Axonics SNM system should be considered as an option for people with refractory overactive bladder, that is, when conservative treatment or treatment with medicine has not worked, in line with NICE's guidelines on urinary incontinence and pelvic organ prolapse and lower urinary tract symptoms. Axonics SNM system is small and does not need to be removed for most types of MRI scans, so it may be useful for people with a low body mass index (BMI) or when an MRI is likely.

1.3 Cost modelling estimates that, over 15 years, Axonics SNM system is cost saving compared with the non-rechargeable system by about £6,025 per person. Cost savings are estimated to begin 6 years after implant. This is because the device needs to be replaced less frequently than the non-rechargeable system, assuming Axonics has a life span of at least 15 years. For more details, see the NICE resource impact statement.

Why the committee made these recommendations

Axonics SNM system uses electrical impulses to stimulate the sacral nerves in the pelvic floor or groin area, to help bladder control. The system is implanted surgically and has a small stimulator that uses a rechargeable battery. Axonics SNM system should be considered when other medicines and treatments do not work.

Axonics SNM system has a longer battery life than the non-rechargeable system used in NHS practice. This means that it needs replacing less frequently, so people need surgery less often. Also, the small size and shape of the stimulator makes it more suitable for

people with a lower BMI than the larger, non-rechargeable system. If people need an MRI, the system does not need to be removed, which means surgery to replace it would not be needed.

Evidence from clinical trials shows that Axonics SNM system improves symptoms of overactive bladder and quality of life.

The cost analysis suggests that using Axonics SNM system may lead to cost savings, but this depends on the length of time the battery lasts. The battery is expected to last at least 6 years, at which point it is estimated that Axonics SNM system becomes cost saving to the NHS.

2 The technology

Technology

2.1 Axonics sacral neuromodulation (SNM) system stimulates the sacral nerve through an implantable pulse generator implanted subcutaneously in the upper buttock. Lead electrodes implanted through the corresponding sacral foramen transmit pulses from the stimulator to the sacral nerves. The stimulator is powered by a rechargeable battery.

A handheld remote control activates the stimulator, adjusts the stimulation amplitude, and checks the battery status. A wireless charger, attachable to the skin over the implanted stimulator, is used to charge the stimulator. The company claims that the battery needs recharging every 1 to 2 weeks for 30 minutes to 1 hour. The implanted device is programmed by a clinician in an outpatient setting using a portable tablet. Axonics SNM system received a CE mark as a class 3 medical device in June 2016.

Innovative aspects

2.2 The rechargeable battery that powers the stimulator has an expected life span of at least 15 years, which the company claims is longer than the comparable non-rechargeable device. The stimulator is compatible with MRI and is smaller than existing non-rechargeable SNM devices, making it more suitable for people with a low body mass index.

Intended use

2.3 The Axonics SNM system is intended to treat symptoms of overactive bladder, urinary retention and chronic faecal incontinence, specifically when conservative treatment and treatment with medicine have not worked or are not suitable. Urinary retention and faecal incontinence are outside the scope of this evaluation. The decision to treat with SNM therapy using the Axonics SNM system is made by a multidisciplinary

team, including surgeons, specialist nurses and physiotherapists, together with the person having the treatment. Axonics SNM system is implanted by surgeons specialising in bladder dysfunction. Limited surgical and patient training is needed.

Costs

2.4 The Axonics SNM device costs £9,660 for the permanent implant.

For more details, see the website for Axonics SNM system.

3 Evidence

Clinical evidence

The main clinical evidence comes from 2 single-arm trials

3.1 Two studies met the inclusion criteria defined by the scope:

- ARTISAN-SNM (McCrery 2019 and Lane 2020; n=129 patients), which included 19 centres in the US and Europe (the Netherlands, Belgium, France and the UK) and had a follow up of 12 months.
- RELAX-OAB (Blok 2018a and b, Blok 2019a and c; n=51 patients), which included 7 centres in Europe (the Netherlands, Belgium, France and the UK) and had a follow up of 2 years.

  Both studies were non-comparative, before and after, intra-patient, observational studies reporting patient outcomes as a change from baseline. Both studies had design and reporting weaknesses. The company also submitted evidence for the non-rechargeable comparator system.

The population and definitions of response to therapy and test response vary in both studies

3.2 ARTISAN-SNM included people with urinary urge incontinence. Response to therapy was defined as at least a 50% reduction in urinary urge incontinence (episodes of urinary leaks) per day according to 3-day urinary diary entries at 6 months. RELAX-OAB included people with urinary urge incontinence (n=37) and all except one had symptoms of urinary frequency (n=50). Although not considered a primary outcome, response to therapy in RELAX-OAB was defined as at least a 50% reduction in episodes of urinary leaks for people with urinary urge incontinence. For people with urinary frequency in RELAX-OAB, response to therapy was defined as at least a 50% reduction in voids or reduction to fewer than 8 voids per day. ARTISAN-SNM defined test response as

symptoms responding to therapy at 1 month after implant. RELAX-OAB defined test response as symptoms responding to therapy at 2 weeks or 1 month after implant.

Clinical outcome data show that Axonics SNM system is effective at improving symptoms of overactive bladder

3.3 ARTISAN-SNM reported a statistically significant reduction in:

- mean daily urinary urge incontinence (episodes of urinary leaks) from 5.6±0.3 at baseline to 1.3±0.2 after 6 months, and 1.4±0.3 at 1 year ($p<0.0001$)
- urinary frequency episodes (average voids per day) from 11.6±0.3 at baseline to 8.7±0.2 at 6 months ($p<0.0001$).

RELAX-OAB reported a reduction in:

- mean daily urinary urge incontinence (episodes of urinary leaks) from 8.3±0.8 at baseline to 1.8±0.5 after 1 year ($p<0.001$) and to 1.7±0.5 at 2 years ($p<0.0001$)
- urinary frequency episodes (average voids per day) from 14.3±1.1 at baseline to 8.0±0.5 at 1 year ($p<0.001$) and 7.3±0.4 at 2 years ($p<0.0001$).

The evidence suggests that symptoms of urinary urge incontinence were more likely to improve than urinary frequency symptoms, but this depended on how improvement was defined. The clinical effectiveness of Axonics sacral neuromodulation (SNM) system was not assessed beyond 2 years.

Studies report an improved quality of life

3.4 Both studies reported scores for the domains of the quality-of-life measure ICIQ-OABqol before and after treatment. ARTISAN-SNM reported an average score improvement of 34 points at 1 year and RELAX-OAB reported an average improvement of 29 points at 2 years. Absolute before and after quality-of-life scores were not reported.

It is likely the battery life of Axonics SNM system will last at least

15 years

3.5 Because there was no long-term clinical evidence, a second independent external assessment centre (Newcastle EAC) assessed the company's technical data supporting the claimed 15-year life span for the battery and the device's compatibility with MRI. The EAC concluded that, if moderate or typical stimulus is maintained for the lifetime of the battery, it is likely that the battery will exceed its claimed life span of 15 years. No evidence was submitted to explore the potential effect of lead migration (that is, when the lead moves from where it was inserted) or if the lead breaks. Minor lead migrations can be compensated for by increasing the stimulus, but major lead migration and breakage need to be corrected by surgery.

Cost evidence

The company's de novo cost model estimates that Axonics SNM system is cost saving in people with symptoms of overactive bladder

3.6 The de novo cost analysis used a Markov model adapted from a previously published model (Noblett 2017) to compare the rechargeable Axonics SNM system with the non-rechargeable system in people with overactive bladder. Most clinical parameters in Noblett 2017 are derived from the 12-month Insite trial (Noblett 2016). The de novo model involved a quarterly progression between 3 health states (on SNM therapy, stopping therapy and death). The model assumed equivalent clinical effectiveness, therapy stopping rates and rate of adverse events for both the rechargeable and non-rechargeable systems, so the same inputs were used for both arms. Results showed that over a 15-year time horizon, using Axonics SNM system in this population is cost saving by £6,038 per person.

The EAC's model includes costs for post-procedure adverse events and the same rate of surgical site infection for Axonics SNM system and the comparator

3.7 The EAC considered that the study central to the company's model (Noblett 2017) had potentially serious limitations in reporting data sources. It noted that it was difficult to identify data stated in the model from the referenced papers. This limitation was partly addressed by an updated reference list submitted by the company. In the EAC's base case, clinical equivalence was not assumed so data on therapy stopping rate and lead migration were taken from Axonics SNM studies for the rechargeable SNM arm of the model. The company model assumed that all adverse events happen in the same cycle as the implant procedure. This was revised because lead migration, lead breakage and pain may not be related to the procedure and may continue throughout the life of the model. The assumption that the implant procedure would need an inpatient admission was changed to a day-case surgery, based on expert advice. A further revision was made to the cost model after consultation to apply the same rate of surgical site infection for both Axonics SNM system and the non-rechargeable comparator (1%).

It is estimated that Axonics SNM remains cost saving after the EAC's revisions to the model

3.8 In the EAC's preferred base case, Axonics SNM system was associated with an estimated cost saving of £6,025 per person over 15 years. A one-way sensitivity analysis showed that the timing of device replacement is a key driver of the cost savings. Threshold analysis showed that Axonics SNM system becomes cost saving when the life span of the technology is 6 years or longer.

4 Committee discussion

Clinical-effectiveness overview

There is a new rechargeable SNM system but it is not an appropriate comparator for this evaluation

4.1 A new rechargeable sacral neuromodulation (SNM) system, InterStim Micro (Medtronic), was launched in the UK when Axonics SNM system was being assessed. The clinical experts explained that InterStim Micro was not yet widely used in the NHS so had not been accepted as standard NHS practice. The external assessment centre (EAC) reported that there was currently no published evidence on InterStim Micro for treating symptoms of overactive bladder. The committee concluded that the appropriate comparator for the Axonics SNM system in this evaluation remained the non-rechargeable SNM system.

Axonics SNM system is clinically effective and improves quality of life

4.2 The committee noted the non-comparative evidence from 2 studies (ARTISAN-SNM and RELAX-OAB) and testimony from a patient survey. Some patients described the technology as 'completely life changing', others felt in control of their condition. The clinical experts said that Axonics SNM system improves symptoms and quality of life. They noted that the test phase programming for both devices was different and that Axonics SNM system had 2 programs available during the test period. The Axonics SNM system permanent implant has 1 program, whereas the standard non-rechargeable SNM system has 4 default programs that a patient can switch across remotely. All programs for both Axonics SNM system and the standard non-rechargeable SNM system can be optimised for individual patients. The permanent implantation procedure is similar for both devices. The committee concluded that Axonics improves symptoms of overactive bladder and quality of life.

The 15-year battery life of the Axonics SNM system is plausible

4.3 The committee noted that there was a lack of long-term follow-up data from the existing studies that validated the company's claim of extended battery life in real-world use. The technical expert explained that battery longevity depends on the recharge interval, charging regime and discharge profile. Newcastle EAC did an assessment of accelerated battery bench testing data submitted by the company. Based on this and expert advice, the committee concluded that it was plausible that the Axonics SNM battery would last 15 years for a person who needs typical stimulus (2.1 milliampere) to manage their symptoms. No data on battery failure were submitted and the committee was also advised that the recharge interval depended on stimulation parameters. Also, some devices may fail within the 15-year life span if stimulus current of up to 4 milliampere is needed to manage symptoms. Mild cases of lead migration were noted as a possible cause of changes in stimulus current. The committee further considered that evidence from RELAX-OAB showed that stimulation amplitude increased up to 3 months after the device was implanted. But, in the longer term, once the lead settles in the body, amplitude may stabilise or decrease. The committee concluded that even though evidence on battery life was limited, it was plausible that the battery would last at least 6 years and possibly beyond 15 years.

Desensitisation may occur with Axonics SNM system, but this is unlikely to be different to the non-rechargeable system

4.4 The clinical experts explained that it was difficult to predict what proportion of people had symptoms that would stop responding over the 15-year life span of the Axonics SNM system. They stated that all treatments for overactive bladder are associated with some level of decline in response. This could be because of the person's lifestyle, loss of efficacy, break in circuit or anticipated changes in the stimulation delivered. Clinical experts advised that a therapy break may be recommended to assess if people should continue to use SNM therapy (rechargeable or non-rechargeable). The committee noted that long-term therapy breaks (for desensitisation or pregnancy) may reduce the rechargeable battery life, but evidence of this was not available. The committee concluded that although desensitisation may occur, this is

unlikely to be different with Axonics SNM system than with the non-rechargeable system.

Side effects and adverse events

There are no reports of serious adverse events with Axonics SNM system

4.5 There was no evidence on adverse events beyond 2 years. The most common minor device-related adverse events related to discomfort associated with stimulation. Clinical experts agreed that discomfort with stimulation can usually be corrected with reprogramming. The committee concluded that no serious adverse events had been reported with Axonics SNM system.

NHS considerations overview

No other medicine or treatments should be needed with Axonics SNM system

4.6 The clinical experts explained that Axonics SNM system is usually used in their practice as a third-line therapy after conservative treatment and treatment with medicine have not worked, which is in line with NICE's guidelines on urinary incontinence and pelvic organ prolapse and lower urinary tract symptoms. They explained that SNM is normally expected to be the only therapy needed to improve symptoms of overactive bladder, but occasionally it may become less effective because of desensitisation. If so, medicine may be needed to control symptoms before making a decision to remove the SNM system. The committee concluded that no other treatments (including medicine) for overactive bladder should be needed with Axonics SNM system, unless symptoms are no longer adequately controlled.

Other patient benefits or issues

Axonics SNM system may benefit people with protected characteristics under the Equality Act 2010

4.7 Overactive bladder is common in women who have been pregnant or who are postmenopausal. It is more common in older people, people with obesity and may be common in disabled people. The instructions state that Axonics SNM system is contraindicated for patients who are unable to operate it. So, the technology may not be suitable for all patients, which could include some disabled people or people with cognitive impairment. The clinical experts explained that the device can be recharged by a carer. The committee noted that when a carer is not available to help with recharging Axonics SNM system, the option of a non-rechargeable SNM system would still be available.

Axonics SNM system has advantages for people with low body mass index or who are likely to need an MRI scan

4.8 The clinical experts said that the smaller size of the Axonics SNM system compared with the non-rechargeable device makes it more suitable for people with low body mass index. Axonics SNM system is conditionally safe to be used with 1.5T and 3T full-body and head coil MRI. The MRI compatibility of the device means that most people with overactive bladder who may need future MRI scanning do not need to have their device removed, avoiding replacement surgery. This consideration was also relevant to people with chronic conditions such as multiple sclerosis, who are likely to need regular MRI scans.

Patient choice is key to deciding whether to use a rechargeable SNM system

4.9 The clinical experts explained that people are told about the advantages and disadvantages of the rechargeable and non-rechargeable systems before a device is implanted. These include uncertainty about device longevity and possible causes for device failure. The longer battery life of Axonics SNM system may appeal to a person using the device. The

committee concluded that this is ultimately the person's decision.

Axonics SNM system is easy to use

4.10 Clinical experts stated that Axonics SNM system is easy to use, for the person and the healthcare professional, and needs little in the way of additional training. They also explained that the implant procedure for the Axonics SNM system is minimally invasive and no more complex than for the non-rechargeable device. A clinical expert explained that people with memory problems may prefer the non-rechargeable device but that people with mild cognitive impairment may be able to have an Axonics SNM system if support is available. The committee concluded that Axonics SNM system could be used by most people, particularly if a carer can help.

Cost modelling overview

The EAC's revised cost model is plausible

4.11 The committee accepted the EAC's preferred cost model, which showed that Axonics SNM system becomes cost saving at 6 years after implant. The committee acknowledged the uncertainties in extrapolating data collected over 2 years to a 15-year time horizon but considered this approach to be suitable for decision making. The committee acknowledged that the failure to include the cost of battery disposal in the cost modelling was a limitation.

The risk of device failure after 1 year should be shared with the company

4.12 The company explained that the device warranty lasts for 12 months. The clinical experts explained that people are advised to include their device in insurance policies to cover loss of, or damage to, the remote or charger. The committee considered that, based on the company's confidence in the longevity of the device and the results of the cost modelling, the warranty should be extended by the company to at least 6 years.

The rates of surgical site infection should be 1% for both Axonics SNM system and the non-rechargeable system

4.13 After consultation, the EAC investigated if other parameters and scenarios affected the cost modelling. The rate of surgical site infection used in the model, which had been different for the Axonics SNM system than the non-rechargeable SNM system, was changed to 1% for both groups. The clinical experts explained that in practice, rates of surgical site infection are low, and they had not seen an obvious difference in surgical site infection rates between Axonics SNM system and the non-rechargeable SNM system. The committee concluded that the rates of surgical site infection used in the model should be the same for both the intervention and comparator technologies. It agreed that 1% was appropriate given the low rate of surgical site infection in clinical practice.

Fewer pain-related events and no cost for the clinician programmer should be included in the cost modelling for Axonics SNM system

4.14 After consultation, the committee considered the suggested changes to the model. The clinical experts explained that Axonics SNM system was smaller than the non-rechargeable system, so it was reasonable to assume that people would have fewer pain-related events. Also, the company explained that the clinician programmer is provided free of charge, so it was correct that no cost for this was included in the model. The committee concluded that fewer pain-related events and no cost for the clinician programmer were appropriate assumptions in the cost modelling.

An appropriate estimate for the lifespan of the non-rechargeable SNM system is 4.4 years

4.15 The committee considered the possible effect of a longer lifespan for the non-rechargeable comparator SNM system on the cost-effectiveness modelling. But the clinical experts explained that 4.4 years accurately reflected their own clinical experiences. The committee concluded that

an estimated lifespan of 4.4 years for the non-rechargeable SNM system was appropriate for the cost-effectiveness modelling.

Main cost drivers

Time to device replacement is key

4.16 The EAC's sensitivity analyses identified time to device replacement as a key driver of cost savings. The committee concluded that Axonics SNM system is cost saving only if it lasts longer than the non-rechargeable device.

Cost savings

Axonics SNM system is cost saving compared with standard care, but more evidence is needed about the battery life beyond 6 years

4.17 The EAC's revised cost modelling estimated that over 15 years, using Axonics SNM system for managing refractory overactive bladder is associated with an estimated cost saving of £6,025 per person in the base case. It showed that cost savings depended on the battery life of Axonics SNM system lasting longer than around 6 years after implant. A battery life of more than 6 years increased the amount of cost savings progressively from 6 years after implant. The committee noted that there was some uncertainty about the battery life beyond 6 years, because there was little published evidence about this. Taking into account Newcastle EAC's technical assessment and expert advice, the committee agreed that the battery is likely to last for at least 6 years. It concluded that Axonics SNM system is cost saving compared with standard care. However, the maximum level of cost savings is uncertain without more evidence about the battery life beyond 6 years.

Further research

Further research and collecting registry data would help address

uncertainties

4.18 Further evidence on the long-term clinical effectiveness, quality-of-life benefits and the device longevity of Axonics SNM system in people with refractory overactive bladder would be welcomed. It is recommended that clinicians routinely collect clinical and procedural outcome data on SNM systems, including Axonics. Ideally this should be a national registry set up with a professional society.

5 Committee members and NICE project team

Committee members

This topic was considered by NICE's medical technology advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of the medical technology advisory committee, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each medical technologies guidance topic is assigned to a team consisting of 1 or more technical analysts (who act as technical leads for the topic), a technical adviser and a project manager.

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