

# Axonics sacral neuromodulation system for overactive bladder and faecal incontinence

Medtech innovation briefing

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## Summary

- The **technology** described in this briefing is the Axonics rechargeable sacral neuromodulation system. It is intended for use in overactive bladder syndrome and faecal incontinence.
- The **innovative aspects** are that it is currently the only rechargeable sacral neuromodulation system and is designed to need less frequent surgical replacement than current non-rechargeable systems.
- The **intended place in therapy** is as an alternative to non-rechargeable sacral neuromodulation devices in people with urinary or faecal dysfunction, who would be offered sacral neuromodulation in line with current NICE guidance.
- The **main points from the evidence** summarised in this briefing are from 1 multicentre, post-marketing study in 51 adults with overactive bladder and 1 case series involving 5 people with faecal incontinence. They show that Axonics may provide effective sacral neuromodulation therapy, and that most people were satisfied with rechargeable therapy. Axonics was not compared with any other treatment.
- **Key uncertainty** around the technology is that the available evidence is limited in quantity and quality, especially for use in faecal incontinence. Well-designed, comparative studies with larger numbers of patients and longer follow-up would be helpful to confirm equivalence to standard care.
- The **cost** of the Axonics sacral neuromodulation system is £475 for the trial phase, £9,210 for a

- permanent implant and £6,500 for a replacement implant (all excluding VAT). The **resource impact** would be similar for initial implantation but, if Axonics is shown to need replacing less often than current sacral neuromodulation systems, there could be less resource use from fewer procedures and associated complications. There is no relevant published evidence to support this.

## The technology

Axonics rechargeable sacral neuromodulation (SNM) system (Axonics Modulation Technologies, Inc.) is an implantable SNM therapy for bladder or bowel control in people with urinary retention, symptoms of overactive bladder or chronic faecal incontinence. SNM (also called sacral nerve stimulation) is a treatment that uses electrical impulses to stimulate the sacral nerves, located in the pelvic floor or groin area.

The Axonics SNM system includes an implantable neurostimulator, tined lead, programmers for use by the clinician and patient, and an external trial system. A wireless charging device is also included for contactless charging of the neurostimulator.

Before permanent implantation, a temporary trial of SNM is recommended to assess the efficacy of therapy. Using the external stimulator, 2 different trial stimulation techniques can be done; a percutaneous nerve evaluation test using the non-tined, single-contact temporary lead or a first-stage, tined lead test using the permanent tined lead.

The company also offers kits containing all surgical tools needed for a percutaneous nerve evaluation test and tined lead implant at extra cost.

## *Innovations*

Axonics is currently the only rechargeable SNM system on the market. It is designed to reduce the number of invasive battery replacement procedures that would be needed every 3 to 5 years with a non-rechargeable system. The Axonics system is also smaller than non-rechargeable SNM devices. This is claimed to help reduce the risk of implant site pain and make it more suitable for people with low BMI.

## *Current care pathway*

NICE's guidelines on [urinary incontinence in women](#) and [lower urinary tract symptoms in men](#) recommend initial management of symptoms with conservative methods (such as behavioural techniques, physical therapies or medication). If symptoms persist, people should be referred to a

multidisciplinary team for specialist urological assessment and management. At this stage, investigations may be done to confirm the presence and involvement of detrusor overactivity, before offering invasive therapy such as SNM. Alternative third-line treatment options include injecting botulinum into the bladder wall, and irreversible surgical procedures such as bladder reconstruction (augmentation cystoplasty), and urinary diversion.

NICE's guideline on [faecal incontinence in adults](#) recommends starting treatment with a combination of conservative interventions (including dietary changes, addressing bowel habits, identifying coping strategies and medication) followed by specialist conservative management (such as pelvic floor muscle training, bowel retraining, specialist dietary assessment and management, biofeedback, electrical stimulation and rectal irrigation) if symptoms persist. If faecal incontinence continues after conservative management, specialist assessments should be done to identify possible causes and assess the patient's suitability for surgery. Surgical treatments include repairing or tightening the sphincter (sphincteroplasty), or a colostomy (for severe uncontrolled faecal incontinence). Neosphincter surgery (graciloplasty or an artificial anal sphincter) may be considered, although these procedures are now very rarely done in the UK. NICE's interventional procedures guidance on [sacral nerve stimulation for faecal incontinence](#) suggests it is an option that is typically offered as a surgical treatment for most patients for whom sphincter repair is inappropriate.

### *Population, setting and intended user*

The Axonics SNM system would be used instead of non-rechargeable SNM systems in line with existing guidelines for urinary or faecal incontinence. As with other SNM devices, patient selection is guided by a positive response to a trial of tined lead testing or percutaneous nerve evaluation.

The system would be started by secondary care multidisciplinary teams including surgeons, specialist nurses and physiotherapists, and implanted by surgeons specialising in bowel or bladder dysfunction.

After implantation, patients use the remote control to adjust the level of stimulation depending on symptom control and comfort. They will also recharge the stimulator when battery level is low (as shown by the patient remote control). The company claims that the device will need recharging for 20 to 60 minutes every 1 to 2 weeks, if standard stimulation settings are used.

## Costs

### Technology costs

The Axonics SNM system, including necessary consumables and accessories, costs between £9,685 and £10,510 (excluding VAT) depending on the type of temporary stimulation used. The cost of replacing the system, which the company estimates is needed every 15 or more years or more often because of battery depletion, is £6,500.

The company has provided a full breakdown of component costs (see [table 1](#), all costs exclude VAT).

All Axonics SNM system components are sold with a 12-month product warranty.

As well as the device costs, healthcare resource associated with implantation is £4,279 for urinary incontinence and £4,431 for faecal incontinence, based on the following Health Resource Group codes:

- Insertion of neurostimulator for treatment of urinary incontinence (LB79Z).
- Insertion of neurostimulator electrodes for treatment of urinary incontinence (LB08Z).
- Insertion of neurostimulator for treatment of faecal incontinence (FZ96Z).
- Insertion of neurostimulator electrodes for treatment of faecal incontinence (FZ97Z).

**Table 1 Cost of Axonics SNM system**

| Description                            | Cost   | Additional information  |
|--|--------|---|
| <b>Trial phase (basic evaluation)*</b> |        |   |
| Trial lead and surgical tools          | £300   | Contains 1 PNE lead and all surgical tools needed for a PNE lead implant. |
| External stimulator                    | £175   | Single-use, disposable external stimulator, 1 belt included.              |
| <b>Permanent implant**</b>             |        |   |
| Neurostimulator                        | £6,500 | Battery life of more than 15 years.                                       |
| Tined lead                             | £1,450 |   |

|   |        |  |
|---|--------|--|
| Permanent lead implant kit  | £200   | Contains all surgical tools needed for a tined lead implant. |
| Patient remote control  | £500   |  |
| Charging system   | £560   | Includes 1 belt and 9 adhesive carriers.                     |
| <b>Replacement Implant</b>  |        |  |
| Neurostimulator   | £6,500 | Battery life of more than 15 years.                          |
| <p>* For advanced evaluation, an additional £1,475 would be needed (trial lead and surgical tools are replaced with tined lead with percutaneous extension [£1,575] and lead implant kit [£200]).</p> <p>** The costs associated with a permanent implant assumes that the patient had a successful basic trial evaluation. In an advanced trial evaluation, the cost associated with permanent implant would be £1,650 less because the tined lead and permanent lead implant kit would not be required.</p> |        |  |
| Abbreviation: PNE; percutaneous nerve evaluation.   |        |  |

### *Costs of standard care*

A standard non-rechargeable SNM device (InterStim II, Medtronic), including necessary consumables and accessories, costs between £9,765 and £9,997 (including VAT) depending on the type of temporary stimulation used. The cost of replacing the system, which is typically needed every 3 to 5 years because of battery depletion, is £7,494.

### *Resource consequences*

If adopted, the Axonics SNM system would be used instead of a standard non-rechargeable SNM device (InterStim II, Medtronic), without needing changes to the current pathway in which SNM therapy is currently delivered in the UK.

The initial costs of implanting the Axonics system are similar to current non-rechargeable systems and, assuming the system needs replacement less often, it could reduce costs for medium- to long-term treatment (more than 5 years).

The company claims the Clinician Programmer accessory, which consists of a touchscreen colour tablet with built-in stimulation capabilities, provides a superior user experience for the surgeon

because it is designed to decrease programming time and the need for manufacturer support.

A cost-consequences study conducted in the US and sponsored by Axonics (Noblett et al. 2017) estimated that using a rechargeable SNM device for the management of overactive bladder syndrome would save \$27,121 per patient over 15 years compared with a non-rechargeable device. Assumptions about the neurostimulator lifetime for the rechargeable device were based on the currently reported lifetime of rechargeable spinal cord stimulation systems. Further economic evidence-based on clinical studies with the Axonics SNM system would be helpful.

## Regulatory information

Axonics rechargeable sacral neuromodulation (SNM) system is CE marked as a class III medical device. Implantable components of the Axonics SNM system (neurostimulator and tined lead) have received conditional labelling for head-coil scanning only in 1.5 Tesla and 3 Tesla MRI environments.

## Equality considerations

NICE is committed to promoting equality, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. In producing guidance and advice, NICE aims to comply fully with all legal obligations to: promote race and disability equality and equality of opportunity between men and women, eliminate unlawful discrimination on grounds of race, disability, age, sex, gender reassignment, marriage and civil partnership, pregnancy and maternity (including women post-delivery), sexual orientation, and religion or belief (these are protected characteristics under the Equality Act 2010).

Faecal and urinary incontinence are associated with the protected characteristics of age, disability, sex and pregnancy. Axonics rechargeable sacral neuromodulation (SNM) system is contraindicated in people who cannot operate the device, which could include people with physical or mental impairment.

## Clinical and technical evidence

A literature search was carried out for this briefing in accordance with the [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](mailto:mibs@nice.org.uk).

## *Published evidence*

One post-market clinical follow-up study involving 51 people with overactive bladder, and a single-centre case series involving 5 people with faecal incontinence, are summarised in this briefing.

Two publications reviewing the procedural and technical considerations of the rechargeable sacral neuromodulation (SNM) device were also identified but are not included in this briefing. One of these was based on 1 clinician's experience of 11 Axonics SNM system implant cases, done at a single Canadian centre. The other was an expert review done by urologists from a centre in the US.

Table 2 summarises the clinical evidence as well as its strengths and limitations.

## *Overall assessment of the evidence*

Two of the publications included in this briefing (Blok et al. 2018a; Blok et al. 2018b) report outcomes from the RELAX-OAB prospective, multicentre post-marketing study of 51 patients. This was designed to confirm safety, efficacy and technical performance of the Axonics SNM system in people with symptoms of overactive bladder. Results from RELAX-OAB suggest that the device is a safe and effective therapy to treat refractory idiopathic overactive bladder, and that patients are able to charge the device and are satisfied overall with rechargeable SNM therapy.

The evidence base for the use of Axonics SNM system in the treatment of faecal incontinence is very limited, consisting of 1 single-centre, case series involving a total of 5 people. Data from this study, which were published in a conference abstract, suggest that Axonics SNM provides satisfactory efficacy, but the findings cannot be fully assessed for statistical or clinical significance.

For both indications, prospective controlled studies comparing clinical outcomes with current standard care in a larger patient population would be useful to confirm equivalence between the 2 SNM devices. Available evidence is based on short-term data with a maximum follow-up of 1 year. An extended follow-up would be desirable, given the intended duration of implant with the rechargeable SNM device.

## **Table 2 Summary of selected studies**

|                     |
|---------------------|
| Blok et al. (2018)a |
|---------------------|

|                                 |   |
|---------------------------------|---|
| Study size, design and location | Prospective, multicentre, single-arm, open-label study involving 51 people with symptoms of OAB in 7 European centres (2 in Netherlands, 2 in Belgium, 2 in France and 1 in the UK).  |
| Intervention and comparator(s)  | Intervention: Axonics rechargeable SNM System (in a single-implant procedure).<br>No comparator.  |
| Key outcomes                    | <p>91% (31/34) of people who responded to therapy during the initial trial period continued to respond to therapy with Axonics at 3 months. People whose OAB responded to treatment showed a statistically significant and clinically meaningful improvement in all aspects of quality of life (ICIQ-OABqol; <math>p &lt; 0.0001</math> for all comparisons). Across all 51 people who had the implant, no serious device-related adverse events or unanticipated adverse events were seen within the 3-month post-transplant period. 19.6% of people experienced device-related adverse events. The most frequent adverse event was discomfort because of stimulation (accounting for 5 events in 4 people [7.8%]), which was resolved with device reprogramming. No surgical intervention was needed because of device- or therapy-related adverse events. One patient's device was explanted because of an infection at the implant site.</p> <p><u>6-month</u> and <u>1-year</u> follow-up data have been published as conference abstracts. 94% of people whose OAB responded to treatment continue to respond to therapy 6 months and 1 year post-transplant, with statistically and clinically significant improvements in quality-of-life measures. Improvement from baseline in ICIQ-OABqol scores were 26.2 and 21.1 points at 6 months and 1 year, respectively (above the minimally important difference of 10 points).</p> |
| Strengths and limitations       | <p>Strengths: multicentre study with a high follow-up rate at 3 months (91%) and prospectively reported outcomes. The study continued to follow all patients for the duration of the study, regardless of trial period response and it used a validated high-quality QoL questionnaire (ICIQ-OABqol).</p> <p>Limitations: non-comparative study and only 1 of the centres was in the UK. The longest published follow-up was 1 year. An extended follow-up may be desirable because of the intended implant duration for this device. Funding for the RELAX-OAB study was provided by the company, Axonics Modulation Technologies, Inc.</p>  |
| Blok et al. (2018) <sup>b</sup> |   |

|                                 |   |
|---------------------------------|---|
| Study size, design and location | Cohort and study design is the same as that reported by Blok et al. (2018)a.  |
| Intervention and comparator(s)  | Intervention: Axonics rechargeable SNM System (implanted in a single procedure).<br>No comparator.  |
| Key outcomes                    | At 3 months, 98% (47/48) of patients charged their neurostimulator without any problems before their follow-up visit. 96% of patients successfully charged as early as within 2 weeks of implant. Average stimulation amplitude across all subjects was 1.8 mA ( $\pm 1.1$ mA). 69% of subjects had $\geq 14$ -day recharge intervals (time between charging) and 98% of patients had $\geq 7$ -day recharge interval. Across all 51 implanted patients, no charging-related adverse events happened. 83% of all implanted subjects and 94% of people whose OAB responded to treatment were satisfied with their therapy. |
| Strengths and limitations       | The strengths and limitations listed for Blok et al. (2018)a also apply. Estimates of battery life and neurostimulator battery recharge intervals were not based on patient-reported or diary-based tracking but were provided by the manufacturer, Axonics Modulation Technologies, Inc.   |
| <u>Dudding et al. (2017)</u>    |   |
| Study size, design and location | N=5<br>Case series involving patients with faecal incontinence considered for SNM.  |
| Intervention and comparator(s)  | Intervention: Axonics rechargeable SNM System.<br>No comparator.  |
| Key outcomes                    | All patients reported a good response to therapy at 1 month post-implantation, defined as a $>75\%$ reduction in episodes of faecal incontinence. The St Mark's continence score was reduced from a mean of 18 at baseline to 5 at 1 month. At 3 months, 4 out of 5 patients continued to benefit from therapy. Recharging was done at a median of 7 days (range: 7 to 10 days) with no patient needing greater than 60 minutes per charging session. No patient reported any problems with recharging the device.  |

|  |  |
|--|--|
| Strengths and limitations  | This is a UK NHS study. It is a single-site case series involving a small sample of people with no comparator group. The statistical and clinical significance of efficacy outcomes were not reported and no baseline demographics were available. |
| Abbreviations: OAB, overactive bladder; ICIQ-OABqol, International Consultation on Incontinence Questionnaire–Overactive Bladder Symptoms Quality of Life; RELAX-OAB, Treatment of refractory overactive bladder with the Axonics SNM system; QoL, quality of life; SNM, sacral neuromodulation. |  |

## Recent and ongoing studies

One ongoing study (active, not recruiting) was identified:

- [ARTISAN-SNM: Axonics sacral neuromodulation system for urinary urgency incontinence treatment](#). ClinicalTrials.gov identifier: NCT03327948. Status: active, not recruiting. Indication: Urinary Urgency Incontinence (UUI). Device: Axonics rechargeable SNM System.

## Specialist commentator comments

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

All of the specialist commentators were experienced with sacral neuromodulation (SNM) therapy and 2 out of 7 had used the Axonics SNM system before.

## Level of innovation

Most of the specialist commentators agreed that the rechargeable battery is the technology's main innovation. One commentator thought the technology was novel whereas another said it was a novel concept only because of its rechargeability and small implant size. Five specialists thought it was a minor variation on current standard care, because the underlying SNM technology and implantation procedure are similar to non-rechargeable SNM devices. Five commentators identified the InterStim system as an alternative technology with a similar function to Axonics; all of whom described InterStim as non-rechargeable. Three of the commentators added that it had a larger implant size. Apart from the InterStim system, no other competing device was identified by the specialists.

## *Potential patient impact*

Most of the commentators thought the longer battery life would provide the largest benefit to patients, and that using the new technology would lead to fewer revision surgeries. One commentator said the technology could be thought of as less invasive because of this. The same commentator, along with 1 other, did not believe it would lead to improved clinical outcomes overall. The smaller implant size was mentioned by 2 commentators who thought this improvement would reduce the risk of device-related pain, as well as improve comfort, although this was said to be speculative.

The constant-current stimulation supplied by the technology was mentioned by 1 commentator who said it implies the same level of stimulation is received, regardless of changes in tissue properties or healing. They added that this could potentially reduce the number of reprogramming visits and the risk of loss of efficacy.

Two commentators thought that younger patients in particular would benefit from the device, because the duration of lifetime SNM therapy would be longer compared with older patients. Another commentator thought that older patients could benefit from the easy-to-use and compact patient equipment, adding that it could reduce complexity for these patients and help improve their understanding of therapy. One of the commentators believed that people with a low BMI would benefit most from the technology because of its smaller implant size. Other commentators did not specify a particular group, but thought that all people having SNM for overactive bladder or voiding dysfunction could benefit from the device.

## *Potential system impact*

Fewer revision operations, as well as fewer outpatient follow-up visits and inpatient visits for implant site pain, were identified as potential system benefits. Three commentators thought the technology would replace current practice, whereas 4 thought it would be an addition to standard care, offered to people depending on the patient's individual preference. One commentator said the technology would cost less than current standard care, whereas 4 thought it would be cost saving in the long term if the battery lasts as long as the company claims it does. The remaining commentators thought it would cost the same as current practice.

All commentators agreed that there would be no need for facility or infrastructure changes to adopt this technology. Product-specific training for clinicians implanting the device and support staff was identified by most commentators, but was thought to be minimal because the implant procedure is comparable to existing SNM devices. One commentator said that the programming is

slightly different but not difficult. One commentator thought that continence nurse specialists may have additional training on teaching patients how to recharge the device. None of the commentators were aware of any safety concerns or regulatory issues.

## *General comments*

Most commentators said that Axonics was not yet widely available in the NHS, but were not aware of any potential barriers to adoption. According to 1 commentator, patients have found the technology easy to master and the remote control simple to use. According to another, patients are happy with the system and have no issues recharging the device. Another commentator thought the sleek and compact design is more appealing for patients. Dexterity and motivation to recharge the battery weekly were practical issues identified by some of the commentators. One commentator thought that the percutaneous nerve evaluation kit would not be widely used by urologists during the trial phase (basic evaluation), because evidence suggests tined lead testing (advanced evaluation) is more effective. One commentator noted that the technology's MRI compatibility was better than the existing SNM device, which is compatible with MRI scans of 1.5 Tesla only (both the Axonics and the Medtronic systems are only compatible with head scans, but the Axonics system allows for more powerful machines, up to 3 Tesla). The need for long-term follow-up data was identified by 4 of the commentators. Real-world evidence around device longevity, comparative studies evaluating the time to revision surgery compared with non-chargeable devices, as well as the long-term effects of using a recharging system next to the body were also mentioned.

## **Specialist commentators**

The following clinicians contributed to this briefing:

- Dermot Burke, associate professor of clinical surgery, St James's Hospital, Leeds, did not declare any interests.
- Mahreen Pakzad, consultant urological surgeon, University College London Hospitals (UCLH), non-financial professional actively involved in 2 ongoing clinical trials involving the Axonics sacral neuromodulation (SNM) system and 1 ongoing trial involving the Medtronic SNM system.
- Andrew Thorpe, consultant urologist, Newcastle upon Tyne Hospitals NHS Foundation Trust, departmental fellowships received from Medtronic from October 2018 to February 2019.
- Karen Nugent, senior lecturer, University of Southampton, Association of Coloproctology

- (Great Britain and Ireland), did not declare any interests.
- Jane Brocksom, senior urology clinical nurse specialist, Leeds Teaching Hospital NHS Trust, British Association of Urological Nurses (BAUN), did not declare any interests.
- Julie Jenks, advanced nurse practitioner, University College London Hospitals (UCLH), paid consultant for Medtronic; position expired end of October 2018.
- Christopher Harding, consultant urological surgeon, Newcastle upon Tyne Hospitals NHS Foundation Trust, British Association of Urological Surgeons (Chairman of Female, Neurological and Urodynamic Urology Subsection), paid speaker fees from Medtronic and Department of Urology, Newcastle upon Tyne Hospitals NHS Foundation Trust received proctoring fees and an educational grant from Medtronic.

## Development of this briefing

This briefing was developed by NICE. The [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.

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