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Rx ONLY

Caution: U.S. Federal law restricts this device for sale by or on the order of a physician
### Label Symbols

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| ![For USA audiences only](image) | For USA audiences only  
Caution: U.S. Federal law restricts this device for sale by or on the order of a physician |
| ![Warning / Caution](image) | Warning / Caution |
| ![Product Literature](image) | Product Literature |
| ![Magnetic Resonance (MR) Conditional](image) | Magnetic Resonance (MR) Conditional |
| ![Industry Canada certification number](image) | Industry Canada certification number |
| ![This device complies with all applicable Australian Communications and Media Authority (ACMA) regulatory arrangements and electrical equipment safety requirements](image) | This device complies with all applicable Australian Communications and Media Authority (ACMA) regulatory arrangements and electrical equipment safety requirements |
| ![US Federal Communications Commission device identification](image) | US Federal Communications Commission device identification |
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Who to Contact for Help

Please contact your doctors if you have questions about your health or the Axonics Sacral Neuromodulation therapy.

Axonics Patient Support

Axonics, located in Irvine, CA (USA) can help to answer questions about your Axonics SNM therapy. Please note that Axonics cannot talk about your medical condition.

Call: +1-877-929-6642
Hours: M-F, 6:00 am - 6:00 pm (Pacific Time)
Indications for use

Axonics SNM therapy for urinary control is indicated for the treatment of urinary retention and the symptoms of overactive bladder, including urinary urge incontinence and significant symptoms of urgency-frequency alone or in combination, in patients who have failed or could not tolerate more conservative treatments.
The Axonics SNM System is contraindicated for the following patients

- Patients who have not demonstrated an appropriate response to test stimulation; or
- Patients who are unable to operate the Axonics SNM System.
Can it Help You?

Millions of people suffer from symptoms of urinary retention, overactive bladder (OAB) including urinary urgency incontinence and significant symptoms of urgency-frequency. These symptoms can be frustrating, embarrassing, and uncomfortable. Axonics Sacral Neuromodulation ("SNM") therapy may ease these symptoms. This therapy is for people for whom other treatments did not work.

Axonics SNM therapy may help you if you have one or all of these symptoms:

- **Urinary urgency incontinence** – involuntary leakage of urine with a sudden, strong need to urinate.
- **Urinary urgency-frequency** – a sudden need to urinate that happens eight (8) or more times a day
- **Urinary retention** – inability to completely or partially empty the bladder

The Axonics SNM System delivers mild electrical pulses to the area of the sacral nerve located near the tailbone. These mild pulses may restore bladder control while not changing normal urinary function.

Stimulation may not cure your urinary symptoms. However, it is expected to reduce your symptoms and improve your day to day life.
What is Axonics SNM Therapy?

Can it Help You?

This therapy is not for treating urinary symptoms in patients with physical blockage of the urinary tract. Blockage may result from benign prostatic hypertrophy, cancer, urethral stricture, or other causes. Additionally, the Axonics SNM therapy is not for:

- patients who have not demonstrated an appropriate response to test stimulation; or
- patients who are unable to operate the Axonics SNM System.

It is up to you and your doctor to decide if you are a good candidate for the Axonics SNM therapy.
What is Axonics SNM Therapy?

Test Stimulation

If you and your doctor believe Axonics SNM Therapy is right for you, you will first undergo a test stimulation period. This will help determine if the therapy reduces your symptoms. For test stimulation, your doctor will choose to either use a temporary lead for up to 7 days or a long-term lead for up to 14 days. The implant procedure may be done in the doctor’s office or in an operating room. The lead will be implanted and you will receive therapy from an external Trial Stimulator at home. A diary of your symptoms will be captured before and during your test stimulation period. This will help your doctor determine if you benefit from the therapy. Your doctor will use the results of your test stimulation period to determine if you should get the full implanted Axonics SNM System.

For more information on trialing the therapy, ask your doctor and refer to the Axonics Trial Guide (110-0077-001).
What is Axonics SNM Therapy?

The System

The Axonics SNM System consists of 4 key parts:

- A small implanted rechargeable Stimulator device that generates mild electrical pulses.
- A long insulated wire that is implanted near the sacral nerve. The wire delivers electrical pulses from the Stimulator to the area of the sacral nerve.
- A small handheld Remote Control device that allows the patient to monitor the Stimulator.
- A wireless Charger that charges the Stimulator battery.

The Axonics Stimulator has a battery that should last for 15 or more years under expected and worst-case stimulation settings.
**Prohibited Medical Procedure**

**Diathermy**
Shortwave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (collectively described as diathermy) CANNOT be performed if you have an implanted Axonics SNM System. Diathermy can transmit energy through the implanted system, potentially causing tissue damage at the location of the implanted electrodes, resulting in severe injury.

**Magnetic Resonance Imaging (MRI)**
The Axonics SNM System is a MRI Conditional system. Refer to “MRI Patient Guidelines for the Axonics Sacral Neuromodulation System” for more information.

**Other Medical Procedures**
Other medical procedures that may adversely affect you and your Axonics SNM System and should be avoided include:

- Lithotripsy
- Monopolar electro surgery
- Microwave and Radio-frequency (RF) ablation
- Radiation therapy over the Neurostimulator
- Ultrasound or scanning equipment
**Electromagnetic interference (EMI)**

Electromagnetic interference is energy generated by equipment found at home, work, or in public that can interfere with the function of the Axonics SNM System. The Axonics SNM System includes features that provide protection from EMI so that most electrical devices encountered in a normal day are unlikely to affect the operation of the Neurostimulator. While everyday electrical devices are unlikely to affect the Neurostimulator, there are strong sources of EMI that may temporarily affect the operation of your stimulator, including anti-theft detectors found in stores used to detect stolen merchandise. If patients encounter any of these electrical devices, they should walk as far away from the sides of the anti-theft detector when passing through.

**At the Airport, Courthouses, etc.**

If patients encounter walkthrough metal detectors or security archways they should walk-through at a normal pace. These detectors should not affect the Stimulator. Hand-held security wands should be passed over the Stimulator quickly and should not affect the stimulator. Full-body security scanners (millimeter wave scanners) are used by the Transportation Security Administration (TSA) and are considered safe in patients that have a stimulator. Additionally, patients should minimize their exposure by not lingering in the immediate area of the security systems. Some anti-theft detectors may not be visible. If patients feel poorly, they should walk away from the area and anti-theft detectors and security scanners.
Warnings

Case Damage
The Neurostimulator, Remote Control and Charger contain batteries with chemicals that can cause bodily harm, including severe burns, if exposed to your body. Do not rupture or pierce the devices or use the device that appears damaged or has visible internal components.

Use of Charger
If swelling or redness occurs near the Charger attachment site, discontinue to the use of Charger and consult your doctor before using the Charger again.
Clinician training

Implanting clinicians should be trained on the implantation and use of the Axonics SNM System. Prescribing clinicians should be experienced in the diagnosis and treatment of lower urinary tract symptoms and should be trained on the use of the Axonics SNM System.

Use in specific populations

The safety and effectiveness of this therapy has not been established for:

- Pregnant women, the unborn fetus, and during delivery
- Pediatric use (patients under the age of 16)
- Patients with neurological disease origins, such as multiple sclerosis or diabetes.
- Bilateral stimulation
Implantation and use of the Axonics SNM System incurs risk beyond those normally associated with surgery, some of which may necessitate surgical intervention. These risks include, but are not limited to the following:

- Adverse change in voiding function (bowel and/or bladder)
- Allergic or immune system response to the implanted materials that could result in device rejections
- Change in sensation or magnitude of stimulation which has been described as uncomfortable (jolting or shocking) by some patients
- Device fracture/failure
- Device migration
- Electrical shock
- Heating or burn at Neurostimulator site
- Infection
- Lack of effectiveness
- Pain or irritation at Neurostimulator and/or lead site
- Reoperation/Revision
- Seroma, hemorrhage, and/or hematoma
- Suspected lead or Neurostimulator migration or erosion
- Suspected nerve injury (including numbness)
- Suspected technical device malfunction
- Transient electric shock or tingling
- Unintended nerve activation
- Undesirable change in pelvic function
Clinical Summary of Expected Results

The safety and effectiveness of the Axonics Sacral Neuromodulation (SNM) System for urinary control was based on

- the results of a prospective, multicenter clinical study designed to evaluate the safety and effectiveness of the Axonics SNM System (IDE number G170100), and
- a systematic review of published clinical studies that evaluated the safety and/or effectiveness of the Medtronic InterStim fully implantable SNM systems.

The Axonics SNM System is similar in design, technology, performance, indications for use, output characteristics, and patient population to the SNM systems evaluated in published clinical studies. The literature review strategy was conducted according to the guidelines and methods suggested by Egger, Smith and Altman in their book “Systematic Reviews in Health Care.”

The result of the systematic review and meta-analysis included 7 articles, representing a total of 1,277 patients implanted with SNM systems. Safety data were reported in a total of 1,111 patients that had SNM system implants, and effectiveness data were reported in a total of 1,075 implanted patients that had SNM system implants. The articles included in the systematic review and meta-analysis included patients with urinary retention (UR) and overactive bladder (OAB). The OAB patients had symptoms of urinary urgency-frequency (UF) and/or urinary urgency incontinence (UUI).
Additionally, safety and effectiveness data for the Axonics SNM System were reviewed from the ARTISAN-SNM study, which was an investigational device exemption (IDE) pivotal study in which 129 patients with urinary urgency incontinence (UUI) were treated with the Axonics SNM System.

Taking these two sources of data together, safety data were evaluated in a total of 1,240 patients that had SNM system implants, and effectiveness data were evaluated in a total of 1,204 patients with SNM system implants.

**Objective of Studies**

Based on nonclinical studies that demonstrated that the Axonics neurostimulator has comparable output characteristics to the InterStim system reported in the literature, the objective of the systematic literature review was to use published clinical literature to provide clinical evidence of the safety and effectiveness of the device for the improvement of UUI, UF, and UR symptoms. In addition, inclusion of safety and effectiveness data from the ARTISAN-SNM study provides direct evidence of the safety and effectiveness of the Axonics SNM System in the treatment of UUI.

Safety was demonstrated by a review of the following sources, which totaled 1,259 patients:

- Review of incidence of complications of the
Clinical Summary

InterStim System from seven literature articles for urinary dysfunction indications. These consisted of two review articles and five original clinical research articles.

- Review of all Adverse Events (AE) from the ARTISAN-SNM study, the IDE pivotal study for the Axonics SNM System, which was conducted in 15 US clinical sites and 5 sites in Western Europe under G170100. The study enrolled 153 patients, of which 129 were implanted with the Axonics SNM System.

**Effectiveness** of the Axonics device was evaluated using the responder rate endpoint (obtained from the literature specific to the improvement of urinary dysfunction with the use of SNM systems and from the ARTISAN-SNM study):

- Responder rate was defined as:
  - For UUI: Proportion of patients that obtained at least a 50% reduction in the number of leaks per day (analyses included all leaks or only urgency leaks)
  - For UF: Proportion of patients that obtained at least a 50% reduction in the number of voids per day or less than 8 voids per day
  - For UR: Proportion of patients that obtained at least a 50% reduction in the volume per catheterization
Summary of Literature Search Strategy
The objective of the literature review was to systematically identify, select, collate and review relevant studies to support the marketing application of the Axonics SNM System. A summary of the literature search strategy and Inclusion/Exclusion (IE) criteria is provided below.

The scientific literature database, Medline/PubMed, was used by Axonics and duplicated by FDA to perform a search for published data relevant to the clinical evaluation of the Axonics SNM System. The search was conducted for literature published through January 15, 2019.

All articles from the published literature were triaged for inclusion based on their suitability prior to full review. Studies were selected for inclusion in this review if the methods section clearly indicated the equivalent neurostimulation system (InterStim) was used in the treatment of urinary and/or bowel dysfunction. These studies were initially selected by Axonics based on the studied endpoints and the safety and effectiveness criteria selected. Systematic meta-analysis reviews, randomized clinical trials and prospective clinical studies were included by Axonics because, these were deemed “to be of the highest data quality”. Individual cohort studies published less than 15 years ago were included, or if the cohort studies were published over 15 years ago and had more than 100 patients, the studies were also included in this search.

The literature search strategy from Axonics, and duplicated by FDA, consisted of the following three steps. FDA added one more step to select articles focused on urinary dysfunction.
that had a clearly defined study design:

1. The Medline database was searched for indexed articles using 21 MeSH terms (Medical Subject Headings, National Library of Medicine) and broad relevant terms for pelvic neurostimulation systems and treatment of fecal and urinary incontinence. After eliminating duplicates, there were 923 articles.

2. The abstract of each article was reviewed and categorized according to the same rigorous inclusion/exclusion criteria used by Axonics. Exclusions eliminated 896 articles resulting in the selection of 27 articles for full review.

Exclusions included: N<100 pts non-randomized (42 articles), N<100 pts, >15 years (83 articles), > 10 years, non-randomized (1 article), animal data (3 articles), technical note/clinician technique (66 articles), case report/series (38 articles), cost assessment (20 articles), disease state (17 articles), dissimilar medical area (7 articles), dissimilar patient population (64 articles), dissimilar device [e.g., tibial] (151 articles), dissimilar indication (53 articles), excluded study type (e.g., bench, retrospective study) (123 articles), intra-device comparison, (2 articles), medicinal substance (16 articles), no abstract (53 articles), no author (4 articles), no clinical data (98 articles), no device evaluation/no device identification (32 articles), patient care management (30 articles) and articles that only included patient physiology/anatomy/demographics (54 articles). Note that the exclusion numbers above add to 957,
because some excluded articles fit in more than one category.

3. Three additional articles were selected from other sources including 2 articles identified from meta-analysis reviews and one more that was found by cross reference (i.e., it was cited in the most current study publication). This step brought the review to a total of 30 articles for full assessment.

4. FDA performed an additional step to exclude articles that focused on bowel dysfunction. FDA also excluded articles on urinary dysfunction that either reported results in a study cohort already included in the literature review or articles that did not have adequate details on study design methodology. In the case of the InSite study, two articles were included (Siegel 2015\textsuperscript{7}, and Siegel 2018\textsuperscript{8}), which reported on two phases of this study. Phase 1 was a randomized controlled trial (RCT) comparing SNM to standard medical therapy (SMT) at 6 months. Phase 2 was a prospective evaluation of the safety and effectiveness of SNM for 5 years. Overall, a total of seven articles were deemed appropriate for inclusion by the FDA. Out of the seven included articles:
   a. All seven had endpoints appropriate for the assessment of safety, and
   b. Six of seven articles provided long-term effectiveness endpoints appropriate to assess improvements in urinary dysfunction.
Evaluation of Safety

FDA evaluated the safety of the Axonics SNM System based on two sources of data, namely the published articles on the use of the InterStim System for urinary dysfunction and a review of any AE from the ARTISAN-SNM study (the IDE study for the Axonics SNM System).

A total of seven published articles on urinary dysfunction were evaluated. These consisted of two review articles (Herbison 2009 and Siddiqui 2008) and five original clinical research articles (Amundsen 2018, Siegel 2015, Siegel 2018, White 2009, van Kerrebroeck 2007). Since patients from Siegel 2015 (InSite Phase 1) were rolled over to Siegel 2018 (InSite Phase 2), only the number of patients from Siegel 2018 are used for calculations of the total number of implanted patients. These articles presented safety data in a total of 1,111 patients that had SNM system implants.

The ARTISAN-SNM study was conducted in 15 US clinical sites under G170100 and evaluated 129 implanted patients. Taking these two sources of data together, a total of 1,240 patients that had SNM system implants were evaluated for safety.

Safety Results from Literature Sources

The literature provided strong evidence to support a low serious AE (SAE) rates for the use of the InterStim System to treat urinary dysfunction. A total of 1,111 patients had SNM system implants.

All AEs and SAEs reported per article are provided in Table 1 below.
**Clinical Summary**

**Table 1**: Adverse Events Reported in the Literature for the InterStim System.

<table>
<thead>
<tr>
<th>Article Reference</th>
<th>Follow up duration</th>
<th>Adverse Events</th>
<th>SAE</th>
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| Amundsen 2018<sup>1</sup> (139 subjects) | 2 years | • Device revision 3%  
• Device removal 8.6%  
• Infection 2.9%  
• Pain 1.4%  
• Procedural pain 6.0% | • NR † |
| Herbison 2009<sup>3</sup> * (219 subjects) | 12 months | • Pain at implant site 15.3%  
• Pain, new 9%  
• Suspected lead migration 8.4%  
• Infection 6.1%  
• Transient sensation of electrical shock** 5.5%  
• Pain, lead site 5.4%  
• Surgical revision 33.3% | • NR † |
| Siddiqui 2010<sup>6</sup> *** (Spinelli 2005: 127 subjects) | 13.8 months | • Lead migration 7%  
• Lead revision performed 3% | • NR † |
| Siegel 2015<sup>7</sup> € (InSite study – Phase 1) (59 subjects with test stimulation, 51 subjects with full system implant) | 6 months | • Change in stimulation, undesirable 10.2%  
• Pain, implant site 8.5%  
• Lead migration/dislodgement 3.4%  
• Infection, implant site 3.4%  
• Surgical intervention† 3.9% | • 0% |
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<th>Article Reference</th>
<th>Follow up duration</th>
<th>Adverse Events</th>
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<tr>
<td>Siegel 2018⁹ (InSite study – Phase 2)</td>
<td>5 years</td>
<td>• Surgical intervention related to tined lead 22.4% (primary safety endpoint)</td>
<td>• Implant site erosion 0.4% §</td>
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<td></td>
<td></td>
<td>• Undesirable change in stimulation 22%</td>
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<td></td>
<td>• Implant site pain 15%</td>
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<td></td>
<td></td>
<td>• Therapeutic product ineffective 13%</td>
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<td></td>
<td></td>
<td>• Implant site erosion 0.4%</td>
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<td></td>
<td></td>
<td>• Other AEs 6%</td>
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<td></td>
<td></td>
<td>• Surgical interventions ***</td>
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<td>o Due to AE 30.9%</td>
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<td>o Due to Battery replacement 33.5%</td>
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<td>o Due to lack or loss of effectiveness 33.5%</td>
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<td></td>
<td>Permanent explant 19.1%</td>
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<tr>
<td>van Kerrebroeck 2007¹¹ ¹</td>
<td>5 years</td>
<td>• New pain/undesirable change in stimulation 28.3%</td>
<td>• NR ‡</td>
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<tr>
<td></td>
<td></td>
<td>• Pain at neurostimulator site 19.8%</td>
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<td></td>
<td></td>
<td>• Pain at lead site 7.9%</td>
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<td>• Infection at lead or neurostimulator site 7.9%</td>
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<td></td>
<td>• Sensation of electric shock ** 7.9%</td>
<td></td>
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<td>• Undesirable change in voiding function 7.2%</td>
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### Clinical Summary

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<th>Article Reference</th>
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<td></td>
<td></td>
<td>• Lead migration 8.6%</td>
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<td>• Technical problems during implant (surgery) 5.3%</td>
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<td>• Device problem 10.6%</td>
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<td></td>
<td>• Other AE 33.6%</td>
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<td></td>
<td>• Surgical intervention 39.5%</td>
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<td>• Device explant 10.5%</td>
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<td></td>
<td></td>
<td>• Device exchange 23.7%</td>
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<tr>
<td>White 2009¹² ²ª</td>
<td>36.9 months</td>
<td>• Pain, implant site 2.9%</td>
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<td>• Device malfunction, secondary to trauma 8.9%</td>
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<td>• Infection 3.5%</td>
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<td>• Post-operative hematoma requiring intervention 1.5%</td>
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<tr>
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<td>• Lead migration 5.9%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Explant due to lack of effectiveness 3.5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Revision due to battery depletion 2%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Elective removal 5%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Overall surgical intervention 30.3%</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>NR ¤</td>
<td></td>
</tr>
</tbody>
</table>

*NR: Rates are not reported by the authors or not meaningful due to small sample size (n < 30).

* Only AEs with >5% occurrence rate were reported by the authors.

**Typically classified as Uncomfortable sensation or stimulation

***Review article referencing multiple original clinical articles;
Clinical Summary

Only one original article (Spinelli 2005) met the IE criteria set for literature review, and data from this article is provided.

Authors reported AE rates in subjects receiving SNM test stimulation.

Authors reported this AE rate in subjects with full system SNM implant.

The sub-categories of Surgical interventions are not mutually exclusive.

This SAE occurred in 1 subject and was resolved.

Device- and therapy-related AE rates are combined and are not mutually exclusive.

As stated earlier, the Siegel 2015 and Siegel 2018 articles reported results from the InSite study. The InSite study was Medtronic’s post-approval study as required by the FDA at the time of approval of a Premarket Approval (PMA) to help assure continued safety and effectiveness of the approved device. Post-approval studies (PAS) are conditions of device approval.

More information on the InSite study for P970004 can be found on FDA’s website: [https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=101911&c_id=335](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma_pas.cfm?t_id=101911&c_id=335)

The enrollment across 38 sites included a total of 571 subjects with a diagnosis of OAB as demonstrated by greater than or equal to eight voids per day and/or a minimum of two involuntary leaking episodes on a 3-day voiding diary. Subjects must have failed or were not candidates for more conservative medical treatments and were 18 years of age or...
older. Additional inclusion/exclusion criteria can be found in Siegel (2015).

As stated above, the InSite study was conducted in two phases – Phase 1 was a prospective, multicenter RCT comparing SNM to SMT at 6 months. Phase 2 of the InSite study was a prospective evaluation of the safety and effectiveness of SNM for 5 years. Siegel (2015) reported results on Phase 1 of the InSite study, and Siegel (2018) reported results on Phase 2 of the InSite study.

The InSite Phase 1 study (Siegel et al, 2015) included 147 randomized subjects (70 to SNM and 77 to SMT). Adverse event data from a total of 59 subjects assigned to the SNM group were available at the 6-month follow-up. There were no unanticipated adverse device effects. Device-related AEs (related to surgery, therapy, device, or implant site) occurred in 30.5% (18/59) of subjects. None of the device-related AEs were serious. The most common device-related AEs in SNM subjects were undesirable change in stimulation 10.2% (6/59), implant site pain 8.5% (5/59), lead migration/dislodgment 3.4% (2/59), and implant site infection 3.4% (2/59). For the 51 SNM subjects with full system implant, the 6-month post-implant surgical intervention rate was 3.9% (2/51).

InSite Phase 2 (Siegel et al, 2018) included 340 subjects who completed the test stimulation, of which 272 received a full system implant. The primary safety objective of the study was to demonstrate that the upper bound of the 95% confidence interval for the cumulative 5-year rate of AEs related to the tined lead requiring surgery was less than 33%. The 5-year
cumulative rate of surgical intervention related to tined lead was 22.4% (95% CI 16.6-27.7), which fulfilled the primary safety objective. There were no unanticipated device-related AEs. In subjects with a fully implanted system, an undesirable change in stimulation was the most common AE, which occurred in 60 of 272 subjects (22%), followed by implant site pain in 40 subjects (15%) and therapeutic product ineffectiveness in 36 subjects (13%). All other device related AEs, which developed upon or after implantation, were reported in fewer than 6% of subjects. One event, implant site erosion, was classified as serious but it resolved. Surgical interventions were also reported, including revision, replacement, and permanent explant of any device component. A subject could have experienced multiple types of surgical interventions and an intervention could have been due to multiple reasons, such as an AE, subject request, lack or loss of effectiveness or battery replacement. Surgical intervention was performed in 84 subjects (30.9%) due to an AE and 91 (33.5%) underwent a surgical intervention due to battery replacement. In all 272 implanted subjects, the permanent explant rate was 19.1% (95% CI 14.1-23.9) at 5 years. The top reason reported by investigators for permanent explant was an AE in 30 of the 272 subjects, (11.0%), which was most often an ineffective therapeutic product (7 of 272 or 2.6%). Other reasons included subject need for magnetic resonance imaging, lack or loss of effectiveness and withdrawal of subject consent. Of the permanent explants, 23 (8.5%) were associated with a lack or loss of effectiveness. Surgical intervention was performed in 91 subjects (33.5%) due to lack or loss of effectiveness after full system implantation.
van Kerrebroeck et al (2007) conducted a prospective, single-arm, multicenter study initiated after FDA approval of InterStim therapy. A total of 163 subjects were enrolled and 152 subjects received the full system implant. Safety data through 5-year follow-up were presented in all implanted subjects, and relatedness to device or therapy was provided. Table 1 above provides AE rates combined across device-related and therapy-related AEs, and as such, an AE may be either device-related or therapy-related or both. There were 102 (67%) subjects who had at least one device- or therapy-related adverse event. Of the AEs, 31 were device-related (24 subjects, 15.8%) and 240 were therapy-related (97 subjects, 63.8%). Most AEs (96%) were resolved by the time the data were analyzed. A total of 60 (39.5%) subjects experienced an adverse event requiring surgical intervention, with 36 (23.7%) requiring device exchange. The system was explanted from 16 subjects due to adverse event or lack of effectiveness.

Amundsen et al (2018) conducted a multicenter, open-label, RCT in 386 women with more than six episodes of UUI over 3 days and inadequately managed by medications. Subjects were assigned to the SNM arm (n=194) or the Botox arm (n=192). Of the 194 subjects assigned to SNM, 139 received full implants, and safety data are reported in these subjects. At 2 years, device revisions occurred in 4/139 (3%) because of decreased effectiveness. Device removal occurred in 12/139 (8.6%) (infection 2.8%, decreased effectiveness 2.8%, subject desire 1.4%, and pain 1.4%). One participant was re-implanted after a resolved surgical site infection. Post-procedure pain was reported in 6% of subjects. Additional
analysis compared all AEs between Botox and SNM groups, and the only observed clinical difference was an increased rate of urinary tract infections in subjects treated with Botox.

White et al (2009) conducted a prospective, longitudinal study in 221 subjects who received test stimulation, of which 202 received full system SNM implants. Subjects had refractory urinary urgency and frequency (n=121), urge incontinence (n=63), or urinary retention (n=37). At a mean follow-up of 36.9 months, 67 subjects (30.3%) had experienced AEs that required surgical interventions at the lead and neurostimulator site. The complications included pain at the site of the neurostimulator in six subjects (2.97%), device malfunction secondary to trauma in 18 (8.9%), infection in seven (3.5%), postoperative hematoma requiring re-exploration in three (1.5%), and lead migration in 12 subjects (5.9%). An additional seven subjects (3.5%) underwent device removal for lack of effectiveness, four subjects (2.0%) required revision secondary to battery expiration, and ten subjects (5.0%) underwent elective removal.

Herbison et al (2009) reported safety data from 3 articles (Hassouna 2000; Jonas 2001; Schmidt 1999) with 219 implanted subjects at 12 months. Only AEs with more than 5% prevalence were reported by the authors. These AEs included pain at the implant site (15.3%), new pain (9.0%), suspected lead migration (8.4%), infection (6.1%), transient sensation of electric shock (5.5%), and pain at the lead site (5.4%). Surgical revision of the implant or leads had to be carried out in 33.3% of the subjects.
Siddiqui et al (2010) was a review article that summarized safety data from six original articles (five full-text, one abstract only). Only one of the articles (Spinelli 2005) met Axonics’ set literature review inclusion/exclusion criteria, and AE data from this study are summarized in Table 1. This article reported AEs in 127 subjects followed up for an average duration of 13.8 months. Lead migration rate as reported at 6 months was 7%, and lead revision was performed in 3% of the cases.

**Safety Results from Axonics Clinical Study**

The ARTISAN-SNM Study was a single arm, prospective, multicenter, unblinded, pivotal study with the primary objective of evaluating the safety and effectiveness of the Axonics SNM System for the treatment of Urinary Urgency Incontinence (UUI), a subtype of OAB. The study was conducted in 15 US Centers (with 97 subjects implanted) and 5 Centers in Western Europe (with 32 subjects implanted).

In this study, subjects were tested intraoperatively for responses suggestive of lead placement near the target sacral nerve, and were then implanted with the permanent implant rather than undergoing the typical SNM trial period (with external stimulator and percutaneous lead). FDA used the outcomes of this study for their evaluation of the safety of the Axonics SNM System at 6 months post-implantation and therapy activation. In McCrery et al (2019)\(^5\), additional study design details are provided.

The primary safety endpoint was the rate of AEs reported in the study.
Clinical Summary

A total of 181 AEs were reported among 80 subjects across the entire study experience. One hundred eighty (180) of the 181 AEs occurred in implanted subjects, and one AE occurred in a subject that was enrolled in the study but not implanted. Of the 180 AEs, seven were SAEs; no SAEs were procedure-related or device-related. Out of the 173 non-serious AEs, 13 were related to the device, and 15 were related to the procedure (as shown in the tables below). One (1) death occurred from complications following multiple perforated diverticulum of the large intestine. The death was not related to the device or procedure. None of the reported AEs was unanticipated.

The total number and percentage of AEs by event category, seriousness, and relatedness to device or procedure is presented in Table 2 and Table 3.
### Table 2: Device Related AEs and SAEs Reported in the ARTISAN-SNM Study.

<table>
<thead>
<tr>
<th>AE Type</th>
<th>Device Related</th>
<th>Serious Device Related</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Events (n)</td>
<td>Subjects (n/N) (%)</td>
</tr>
<tr>
<td>Proctalgia</td>
<td>1</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Pain</td>
<td>1</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Medical device discomfort</td>
<td>1</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Implant site pain</td>
<td>2</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Incision site infection</td>
<td>1</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Pain at extremity</td>
<td>2</td>
<td>2 (1.6)</td>
</tr>
<tr>
<td>Groin Pain</td>
<td>1</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Dysesthesia</td>
<td>1</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Lead dislodgement</td>
<td>1</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Vulvovaginal pain</td>
<td>1</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td>Vulvovaginal discomfort</td>
<td>1</td>
<td>1 (0.8)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>13</strong></td>
<td><strong>13 (10.1)</strong></td>
</tr>
</tbody>
</table>
### Table 3: Procedure Related AEs and SAEs Reported in the ARTISAN-SNM Study.

<table>
<thead>
<tr>
<th>AE Type</th>
<th>Procedure Related</th>
<th>Subjects (n/N) (%)</th>
<th>Serious Procedure Related</th>
<th>Subjects (n/N) (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>1</td>
<td>1 (0.8)</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Implant site pain</td>
<td>1</td>
<td>1 (0.8)</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td>1</td>
<td>1 (0.8)</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Allergy to chemicals</td>
<td>1</td>
<td>1 (0.8)</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Incision site infection</td>
<td>1</td>
<td>1 (0.8)</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Fungal infection</td>
<td>1</td>
<td>1 (0.8)</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Procedural pain</td>
<td>4</td>
<td>4 (3.1)</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Incision site pain</td>
<td>1</td>
<td>1 (0.8)</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Paraesthesia</td>
<td>1</td>
<td>1 (0.8)</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Keloid scar</td>
<td>1</td>
<td>1 (0.8)</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Dermatitis papillaris capillitii</td>
<td>1</td>
<td>1 (0.8)</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td>Suture insertion</td>
<td>1</td>
<td>1 (0.8)</td>
<td>0</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>15</strong></td>
<td><strong>13 (10.1)</strong></td>
<td><strong>0</strong></td>
<td><strong>0 (0.0)</strong></td>
</tr>
</tbody>
</table>

**Note:** A total of 15 events occurred in a total of 13 subjects.

The most common device-related AEs were implant site pain (n=2), extremity pain (n=2) and vulvovaginal pain/discomfort (n=2). No other device related AE occurred more than once. The most common procedure-related AE was procedural pain (n=4). No other procedure-related AE occurred more than once.
There were no device- or procedure-related SAEs.

The time course and resolution status of device-related and procedure-related AEs from the ARTISAN-SNM study are provided in Tables 4 and 5 below. All AEs and their resolution status are reported as of the data lock date of 18 January 2019.

**Device-related adverse events**

<table>
<thead>
<tr>
<th>Table 1: Summary and time-course device-related adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of implanted subjects = 129</td>
</tr>
<tr>
<td>AE Type</td>
</tr>
<tr>
<td>Implant to 2 Weeks</td>
</tr>
<tr>
<td>--------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Proctalgia</td>
</tr>
<tr>
<td>Pain</td>
</tr>
<tr>
<td>Medical device discomfort</td>
</tr>
<tr>
<td>Implant site pain</td>
</tr>
<tr>
<td>Incision site infection</td>
</tr>
<tr>
<td>Pain in extremity</td>
</tr>
<tr>
<td>Groin pain</td>
</tr>
<tr>
<td>Dysaesthesia</td>
</tr>
<tr>
<td>Lead dislodgement</td>
</tr>
<tr>
<td>Vulvovaginal pain</td>
</tr>
<tr>
<td>Vulvovaginal discomfort</td>
</tr>
</tbody>
</table>

* Includes events that were resolved with sequelae
Procedure-related adverse events

Table 5: Summary and time-course of procedure-related adverse events

<table>
<thead>
<tr>
<th>AE Type</th>
<th>Number of implanted subjects = 129</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total events</td>
<td>10</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>13/2</td>
</tr>
<tr>
<td>Vomiting</td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1/0</td>
</tr>
<tr>
<td>Implant site pain</td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1*/0</td>
</tr>
<tr>
<td>Hypersensitivity</td>
<td></td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1/0</td>
</tr>
<tr>
<td>Allergy to chemicals</td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1/0</td>
</tr>
<tr>
<td>Incision site infection</td>
<td></td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1/0</td>
</tr>
<tr>
<td>Fungal infection</td>
<td></td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1/0</td>
</tr>
<tr>
<td>Procedural pain</td>
<td></td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>3/1</td>
</tr>
<tr>
<td>Incision site pain</td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1/0</td>
</tr>
<tr>
<td>Parasthesia</td>
<td></td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0/1</td>
</tr>
<tr>
<td>Keloid scar</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1*/0</td>
</tr>
<tr>
<td>Dermatitis papillaris capillitii</td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1*/0</td>
</tr>
<tr>
<td>Suture insertion</td>
<td></td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>1/0</td>
</tr>
</tbody>
</table>

* Includes events that were resolved with sequelae
Clinical Summary

Evaluation of Effectiveness

The analysis of effectiveness for the treatment of urinary dysfunction was based on a review of six of the seven articles discussed above for safety. The study by White et al (2009) was excluded from effectiveness evaluation since this study did not provide data on long term effectiveness results. Since subjects from Siegel 2015 (InSite Phase 1) were rolled over to Siegel 2018 (InSite Phase 2), only the number of subjects from Siegel 2018 are used for calculations of the total number of implanted subjects. The six articles encompassed 1,075 subjects with SNM system implants. Additionally, effectiveness data from the ARTISAN-SNM study, with 129 implanted subjects, is included in the effectiveness analysis. Taking these two sources of data together, there were 1,204 implanted subjects evaluated for effectiveness.

Effectiveness Results from Literature Sources

The articles included in the systematic review and meta-analysis included subjects with UR and OAB. The OAB subjects had symptoms of UUI and/or UF.

Key effectiveness outcomes from the published literature on the InterStim System are presented in Table 6 below.
Table 6: Effectiveness Outcomes Reported in the Literature for the InterStim System.

<table>
<thead>
<tr>
<th>Article Reference</th>
<th># Subjects Receiving Test Stimulation</th>
<th># Subjects Receiving Permanent Implant (% of subjects receiving test stimulation)</th>
<th>Follow up Duration with Permanent Implant</th>
<th>Effectiveness Endpoint (Responder Rate)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amundsen 2018</td>
<td>169 (UUI)</td>
<td>139 (82%)</td>
<td>2 years 122 subjects (88%)</td>
<td>50%*</td>
</tr>
<tr>
<td>Herbison 2009**</td>
<td>NR</td>
<td>278 (NR)</td>
<td>NR</td>
<td>Details in Text</td>
</tr>
<tr>
<td>Siddiqui 2010***</td>
<td>NR</td>
<td>234 (OAB) (52-77%¥)</td>
<td>6 months-29 months</td>
<td>45% of subjects reported a lack of daily incontinence episodes</td>
</tr>
<tr>
<td>Siegel 2015 (InSite study – Phase 1)</td>
<td>59 (OAB) 29 (UUI) 19 (UF)</td>
<td>51 (86%)</td>
<td>6 months 51 subjects (100%)</td>
<td>76% (OAB) 71% (UUI) § 61% (UF) Complete continence in 39% of UUI subjects</td>
</tr>
<tr>
<td>Siegel 2018 (InSite study – Phase 2)</td>
<td>340 (OAB) 202 (UUI) 189 (UF)</td>
<td>272 (80%)</td>
<td>5 years 150 (OAB) (55%) 118 (UUI) 109 (UF)</td>
<td>82% (OAB) 76% (UUI) § 71% (UF) Complete continence in 45% of UUI subjects</td>
</tr>
<tr>
<td>van Kerrebroeck 2007</td>
<td>163 103 (UUI) 28 (UF) 31 (UR)</td>
<td>152 (93%) 96 (UUI) 23 (UF) 31 (UR)</td>
<td>5 years 105 subjects (69%) 65 (UUI) 27 (UF) 13 (UR)</td>
<td>58% (UUI) § 40% (UF)† 71% (UR)</td>
</tr>
</tbody>
</table>
Clinical Summary

*Responder rate estimated from graph provided in the article
**Number of subjects with the full system implanted was not provided in the review article and was calculated by Axonics based on data in original clinical research articles
***Authors reported effectiveness data based on three most representative studies.
* This rate was reported in the article
§ Analysis performed on all leaks episodes
† Responder rate was calculated using only one of the two standard criteria used for UF effectiveness. Only criteria of ≥50% reduction in voids as compared to baseline was used; the criteria of reduction to less than 8 voids was not used.
NR: Not reported

As stated in the Safety Section above, two articles (Siegel 2015 and Siegel 2018) presented results of the InSite study. Siegel (2015) reported results on Phase 1 of the InSite study, and Siegel (2018) reported results on Phase 2 of the InSite study. Phase 1 was a prospective, multicenter RCT comparing SNM to SMT at 6 months. Phase 2 of the InSite study was a prospective evaluation of the safety and effectiveness of SNM for 5 years.

Siegel, et al (2015) included 147 randomized subjects (70 to SNM and 77 to SMT). Fifty-nine (59) subjects received SNM test stimulation, of which 51 received the full SNM implant and were available at the 6-month follow-up. Seventy-three (73) subjects received SMT and were available at the 6-month follow-up. Results are reported as the proportion of subjects with both UUI and UF that had a minimum of a 50% reduction in urinary incontinence episodes or voids per day or a return to 8 voids (normal voiding). Two types of analyses were performed – an Intent to Treat (ITT) analysis was
performed based on subject assignment to the randomized group; and an “as treated” analysis was performed based on the treatment received, and in subjects who had both baseline and follow-up visit data. The ITT OAB responder rate at 6 months was 61% in SNM subjects and 42% in SMT subjects. The as treated OAB responder rate at 6 months was 76% in the SNM group and 49% in the SMT group. In the SNM group, 39% of subjects achieved complete continence. The responder rate in UUI subjects was 71% and in UF subjects was 61%. This study provided level 1 evidence of the objective and subjective superiority of SNM over standard medical therapy in subjects with OAB.

Siegel, et al (2018) reported results on Phase 2 of the InSite study, which included a larger cohort and longer follow-up duration. The 2018 study had an initial enrollment of 340 subjects with OAB that underwent test stimulation, of which 202 had UUI and 189 had UF. Among these subjects, 272 (80%) received a full system implant of the SNM device. Of the 272 OAB subjects that received a full system implant, 150 completed the 5-year follow-up visit, of which 118 were UUI subjects and 109 were UF subjects. Responder rates at 5 years were analyzed using two methods. The Modified completers analyses included all subjects who received a full system implant and completed a baseline and 5-year follow-up visit or were exited prior to 5-years due to device-related AE or lack of effectiveness (n=183). The Completers analyses comprised all subjects who received an implant and completed a baseline and 5-year follow-visit (n=150). Using the Modified completers analysis, the 5-year responder rate was 67% in OAB subjects, 64% in UUI subjects and 57% in UF
subjects. Complete continence was achieved in 38% of the UUI subjects. Using the Completers analysis, the 5-year responder rate was 82% in OAB subjects, 76% in UUI subjects and 71% in UF subjects. Complete continence was achieved in 45% of the UUI subjects.

Amundsen, et al (2018) reported results from the ROSETTA trial, which included randomized subjects with UUI (194 to SNM and 192 to Botox (BTX)). One hundred and sixty-nine (169) subjects received SNM test stimulation and subjects who reported $\geq 50\%$ reduction from baseline in UUI episodes continued to the SNM implant stage. Of the 169 test stimulation subjects, 139 (82%) underwent full SNM system implant. One hundred and fifty-nine (159) subjects were BTX clinical responders following one-month injection and continued to be followed for effectiveness. Follow-up duration was 2 years, and 122 SNM subjects and 138 BTX subjects provided diary data at the 2-year visit. Intent to treat responder rate at 2 years for SNM treatment was reported as 50%. The low responder rate in this study may be due use of ITT analysis, which is the most conservative type of analysis. Overall, the authors concluded that both SNM and BTX treatments resulted in similar improvement of UUI episodes at 2 years.

van Kerrebroeck, et al (2007) included 163 subjects enrolled with urinary dysfunction. Of these subjects, 103 had UUI, 28 had UF, and 31 had UR. The majority of these subjects (129) had been implanted with the SNM device as part of a previous clinical trial (MDT-103) and were crossed over to this long-term follow-up study. The remaining 34 subjects were newly enrolled in this study of which 23 received the
full SNM system implant. A total of 152 subjects with full implants were followed for a duration of 5 years. One hundred and five (105) subjects (69%) completed the 5-year follow-up visit, of which 87 reported voiding diary results. SNM therapy success was measured by $\geq 50\%$ improvement from baseline in voiding diary variables. At 5 years, UUI subjects demonstrated a responder rate of 58% (for leaks per day), and UF subjects achieved a responder rate of 40% (for voids per day). UR subjects had a responder rate of 58% (for catheterizations per day) and 71% (for volume per catheterization). Note that even though the standard literature-based criteria for UF responder rate is defined as $\geq 50\%$ reduction in voids as compared to baseline or reduction to less than eight voids per day (normal voiding), this article used only the criteria of $\geq 50\%$ reduction in voids as compared to baseline for calculating responder rate. This may explain the lower responder rate for UF subjects in this study as compared to other studies.

Herbison, et al (2009) includes a review of eight articles reporting effectiveness of SNM treatment for urinary dysfunction. Seven of the eight articles reported results from studies that randomized subjects to an immediate SNM implant group and delayed SNM implant group, and results from the immediate implant group were provided by the authors. Effectiveness results were reported in a total of 278 implanted subjects across the eight articles. Seven of the eight studies reported a subject follow-up duration of 6 months, with the remaining one study reporting follow-up results from 12 months. The review article reported highly significant changes in all reported effectiveness outcomes.
Siddiqui, et al (2010) reviewed literature pertaining to effectiveness of SNM treatment for OAB subjects. Seven studies met the criteria of “good” quality. Three of these studies were designated as most representative by the authors and were included in the effectiveness reporting in Table 6. In these three studies, 234 (52-77%) subjects received full implants following a successful test stimulation period. Follow-up duration ranged from 6 months to 29 months. At the follow-up visits, approximately 45% of subjects reported a cure or lack of UUI episodes.
Effectiveness Results from Axonics Clinical Study

As stated above, Axonics performed a pivotal study, ARTISAN-SNM, to establish the safety and effectiveness of SNM therapy with the Axonics SNM System in subjects with UUI. A total of 129 subjects with UUI were implanted with the Axonics System in the ARTISAN-SNM study.

Effectiveness of SNM therapy was evaluated based on subject bladder diary symptoms at follow-up compared to baseline, as well as improvement in quality of life and subject satisfaction. All effectiveness analyses were performed using an “as treated” analysis, such that subjects with missing data at the follow-up visit were conservatively considered as treatment failures. Specifically, data from three subjects that exited prior to 6 months were missing and their data were imputed using their baseline diary and questionnaire data.

Table 7 and Table 8 present effectiveness results in 129 implanted subjects from the ARTISAN-SNM study.

Treatment responder rate:
The primary effectiveness endpoint was the “as treated” responder rate in all implanted subjects, with a responder being defined as a subject with at least 50% reduction in their UUI symptoms.

At 6-months, 116 of the 129 implanted subjects (89.9%) were treatment responders. The ARTISAN-SNM study met its primary effectiveness endpoint.
Symptom reduction:
The average daily number of urgency leaks decreased from 5.6 ± 3.4 at baseline to 1.3 ± 2.0 at 6 months, a reduction of 4.3 ± 3.3, representing a statistically significant improvement of 76.1% (p<0.0001, lower bound of CI: 3.8) (Table 8).

An analysis was performed in the 6-month treatment responders (n=116) to determine the magnitude of urgency leak reduction. At 6 months, 80.2% of treatment responders (93 of 116) experienced ≥ 75% reduction in urgency leaks. Further, 50.0% of the treatment responders (58 of 116) had ≥ 90% symptom reduction, and 33.6% of treatment responders (39 of 116) were dry (100% symptom reduction).

Planned analyses were performed to test the effectiveness of SNM on large leaks and urgency episodes. The average daily number of large leaks with urgency decreased from 1.0 ± 1.7 at baseline to 0.1 ± 0.4 at 6 months, an average

### Table 7: Responder rate in all implanted subjects

<table>
<thead>
<tr>
<th>Effectiveness Measure (N=129)</th>
<th>Responder Rate</th>
<th>Reject Null Hypothesis?</th>
<th>95% CI</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Responder rate in all implanted subjects at 6 months (As Treated)</td>
<td>89.9%</td>
<td>Yes</td>
<td>(83.4%, 94.5%)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

*One-sided binomial test for responder rate >50%.

Clinical Summary
reduction of 0.9 ± 1.6, representing a statistically significant improvement of 75.4% (p<0.0001, lower bound of 97.5% CI: 0.6).

Average daily urgency was calculated across all diary episodes with at least mild urgency. The average daily number of urgency episodes decreased from 10.6 ± 3.7 at baseline to 6.9 ± 3.4 at 6 months, a reduction of 3.7 ± 3.7, representing a statistically significant improvement of 32.1% (p<0.0001, lower bound of 97.5% CI: 3.0).

Patients were classified as suffering from UF if the bladder diary showed eight or more voids per day. One hundred and three (103) study patients met the criteria of having UF based on their baseline diary. The average daily number of voids decreased from 11.6 ± 3.1 at baseline to 8.7 ± 2.5 at 6 months, a reduction of 2.8 ± 3.0, representing an improvement of 22.4%.

**Quality of life and subject satisfaction:**

The International Consultation on Incontinence Questionnaire Overactive Bladder Quality of Life Module (ICIQ-OABqol) is a validated quality-of-life questionnaire designed to provide a robust assessment of the impact of OAB symptoms in subjects’ lives. It consists of 26 questions and assesses quality of life across four subscales (Concern, Coping, Sleep, and Social Interaction). Per the scoring guidelines, patients’ answers to the questions in each subscale are summed and transformed into scores ranging from 0 to 100, with a higher score indicative of better quality of life. The subscale scores are combined and normalized
into a total health related QoL score (HRQL), also on a scale from 0 to 100. An improvement of 10 or more points is indicative of a clinically meaningful improvement (Jaeschke et al, 1989; Siegel et al, 2016).

Table 8 shows the ICIQ-OABqol HRQL score for baseline and follow-up visits. At the 6-month follow-up, the score was 85.6 ± 15.6, a clinically and statistically meaningful improvement of 34.2 ± 24.7 points from baseline (p<0.0001, lower bound of 97.5% CI: 29.9).

Subjects improved on all aspects of QoL, as reflected by improvements on each QoL subscales: 38.6 points on Concern, 38.6 points on Coping, 31.4 points on Sleep, and 22.6 points on Social Interaction.

Furthermore, subjects reported high rates of satisfaction with their SNM therapy. Ninety-three percent (93%) of the 129 participants responded at 6 months as “satisfied” with the therapy, and 92% responded that they would undergo the therapy again.
**Clinical Summary**

Table 8: Secondary effectiveness results in all implanted subjects

<table>
<thead>
<tr>
<th>Effectiveness Measure (n=129)</th>
<th>Baseline</th>
<th>6-months</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average Daily Number of Urgency Leaks</td>
<td>5.6 ± 3.4</td>
<td>1.3 ± 2.0</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Average Daily Number of Large Urgency Leaks</td>
<td>1.0 ± 1.7</td>
<td>0.1 ± 0.4</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Average Daily Number of Urgency Episodes</td>
<td>10.6 ± 3.7</td>
<td>6.9 ± 3.4</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>ICIQ-OABqol HRQL Score</td>
<td>51.5 ± 22.3</td>
<td>85.6 ± 15.6</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Average Daily Number of Voids (in subjects with at least 8 voids per day at Baseline, n=103)</td>
<td>11.6 ± 3.1</td>
<td>8.7 ± 2.5</td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>ICIQ-OABqol HRQL Score</td>
<td>51.5 ± 22.3</td>
<td>85.6 ± 15.6</td>
<td>&lt;0.0001*</td>
</tr>
</tbody>
</table>

Data displayed are mean ± standard deviation. Missing data at 6-months is imputed with baseline data.

*Two-sided paired t-test for reduction from Baseline

**Two-sided Wilcoxon signed rank test for paired observations for reduction from Baseline
Conclusions
The results compiled from the literature available for the approved Medtronic InterStim SNM System show that SNM therapy provides a clinically meaningful benefit in a significant proportion of patients with urinary retention and the symptoms of OAB who have failed or could not tolerate more conservative treatments and have demonstrated at least a 50% improvement (reduction) in urinary symptoms during a trial period. Effectiveness, as measured by clinically meaningful improvements in urinary symptoms (including reduction in urgency leak episodes, reduction in urgency episodes, reduction in daily voiding frequency, reduction in catheterization volume, reduction in catheterization frequency, and/or improvement in health-related quality-of-life scores), was demonstrated in the referenced articles involving the use of the InterStim SNM System and in the Axonics-sponsored ARTISAN-SNM clinical study of the Axonics SNM System. Given (1) the similarities in design, technological characteristics, non-clinical performance, indications for use, methods and conditions of use, and intended patient population between the InterStim SNM System and the Axonics SNM System, and (2) the data from the ARTISAN-SNM clinical study, which showed similar outcomes relative to what is summarized in the body of clinical literature describing the InterStim System’s clinical performance, it is reasonable to conclude that the Axonics SNM System will have similar clinical performance to that of the InterStim System.

Risks associated with the Axonics SNM System are based on
Clinical Summary

all of the nonclinical laboratory and animal studies conducted on the device, in combination with safety data collected in the Axonics-sponsored ARTISAN-SNM clinical study. Additional risk information, including long-term safety data, was leveraged from a systematic literature review of the similar InterStim SNM System.

In the ARTISAN-SNM study of the Axonics SNM System, there were no serious device- or procedure-related AEs reported. Thirteen (13) (10.1%) of the 129 implanted subjects had 13 device-related AEs, and 13 (10.1%) of subjects had 15 procedure-related AEs. The most common device-related AEs were implant site pain (n=2), extremity pain (n=2), and vulvovaginal pain/discomfort, (n=2). No other device-related AE occurred more than once. The most common procedure-related AE was procedural pain (n=4). No other procedure-related AE occurred more than once.

Of the InterStim safety articles discussed above, the Siegel (2018) article (InSite Phase 2 study) had the longest duration of follow-up and the greatest number of implanted subjects. That study collected up to 5 years of follow-up data on 272 subjects implanted with the InterStim System. An undesirable change in stimulation was the most common AE, which occurred in 60 of 272 subjects (22%), followed by implant site pain in 40 subjects (15%), and therapeutic product ineffectiveness in 36 subjects (13%). All other device related AEs, which developed upon or after implantation, were reported in fewer than 6% of subjects. One event, implant site erosion, was classified as serious but it resolved. Surgical interventions were also reported, including revision,
replacement, and permanent explant of any device component. Surgical intervention was performed in 84 subjects (30.9%) due to an AE, 91 subjects (33.5%) underwent a surgical intervention due to battery replacement, and 91 subjects (33.5%) underwent a surgical intervention due lack or loss of effectiveness after full system implantation. In all 272 implanted subjects, the permanent explant rate was 19.1% (95% CI 14.1-23.9) at 5 years. In the other referenced studies of the InterStim System that provided safety information, there were reported occurrences of additional AE types including infection, lead migration, and transient sensation of electrical shock.

The evidence supporting the safety and effectiveness of the Axonics Sacral Neuromodulation System is based on a foundation of over 20 years of clinical research and experience as documented in the literature with fully implantable SNM systems, the similarities of the Axonics SNM System to the approved InterStim SNM System, and the results from comprehensive nonclinical and clinical testing showing that the Axonics SNM System performs as intended.

Note on Limitation of the Data
The effectiveness of SNM therapy and the Axonics SNM System is based on published studies from medical journals and results from an open label study sponsored by Axonics. In these studies, subjects were aware they were receiving sacral neuromodulation therapy and the studies did not assess whether or not there was a significant placebo response. This may result in overestimation of therapy results.
References


7. Siegel S, Noblett K, Mangel J, et al. Results of a prospective, randomized, multicenter study evaluating sacral neuromodulation with InterStim therapy compared to standard medical therapy at 6-months in subjects with mild
Clinical Summary


The Axonics SNM System will be implanted in an operating room. You may be given general anesthesia or a mild anesthetic along with local sedation.

The doctor will insert a needle just above the tailbone to locate the sacral nerve. Test stimulation will be used to test the needle location and the nerve response. Your doctor will look for muscle responses in your buttocks and big toe. The muscle responses confirm that the needle is stimulating the correct nerve. If you are under local anesthesia, the doctor may ask you how the stimulation feels. You may feel a “pulling” or “tingling” in the pelvic muscles or big toe. Women may feel the stimulation in the vaginal area. Men may feel the stimulation in the scrotum. Some patients feel no sensation at all. Then the lead will be implanted where the needle was placed. Medical imaging (x-ray for example) may be used to confirm the location of the lead.

Next the Stimulator will be implanted, usually in the upper buttock area and always under the skin. Before the procedure, you should talk with your doctor about where the Stimulator will be implanted. The Stimulator will be connected to the implanted lead.

Patients usually go home on the same day as the procedure.
The Procedure

You may feel some pain or discomfort in the first couple of weeks after surgery in the area of the implant as your skin heals. Your doctor may also give you drugs to help with pain. Your doctor or their staff will give you detailed instructions on what to do following your surgery.

In the first few weeks after your procedure, limit your activities. Limiting activities will help you avoid the moving of your implanted lead. This helps ensure that therapy will be effective. When cleared by your doctor, you can go back to regular day to day activities. You will need to continue to avoid some extreme activities (see the section of this guide on “Physical Activity Precautions”).

Note: Similar to any surgical procedure, there are risks with this procedure. Risks include bleeding, bruising, swelling, and infection. Please discuss the procedure and any concerns with your doctor.
Tracking Your Symptoms

A diary is used to track your symptoms. You will need to fill out a diary for several days before and after your System is implanted. The diary provides important information to your doctor that helps your doctor decide if you could benefit from Axonics SNM therapy. It is important to fill out the diary when symptoms occur.

You should carry your diary with you when you are tracking your symptoms and use the diary to record symptom data. Please always bring your diary with you to your doctor visits.

Your doctor, or their staff, will show you how to complete your diary. You should contact them if you have questions.
Living with the Axonics SNM System

What to Expect

Your Stimulator may be turned on when you leave the hospital or very soon thereafter. You may feel a similar sensation as what you felt during test stimulation. It should not be uncomfortable or painful. You should feel a small amount of sensation at all times, and you should increase your stimulation amplitude if you are not feeling sensation.

Stimulation should be on for 24 hours per day, 7 days per week.

If your therapy feels uncomfortable or painful, your doctor can change the stimulation. It may take more than one try by your doctor to find a stimulation setting that gives you both comfort and good symptom relief.

The following items are important for managing your Axonics SNM System:

- Follow-up visits
- Your patient ID card
- Precautions about physical activity
- Precautions about medical procedures
- Precautions about electromagnetic interference
- Your Remote Control
- Recharging your Stimulator

Note: The feeling of your stimulation can change over time. Contact your doctor if your stimulation becomes uncomfortable or if your symptoms worsen.
Support Resources

There are resources to help you live with your Axonics SNM System.

Training
You will be trained on how to use your Remote Control and how to charge your Stimulator by your doctor’s staff. You will also be told about the precautions and warnings to be aware of. If you have questions or problems using your system, ask your doctor and his or her staff for more training.

Patient Identification (ID) Card
You will be given a patient ID card that contains basic information about you and your System. Your patient ID card shows that you have an implanted Stimulator if you have an emergency.

If you lose your patient ID card, please contact Axonics for a new card.
Follow-up Visits

You will have regular doctor visits to check on your health and the Axonics SNM System. Your doctor will help with problems and may change your stimulation settings. If you want to stop therapy you should discuss this with your doctor. Your doctor may or may not advise removal of the Axonics SNM system.

Please bring your Remote Control to your follow-up visits.
Physical Activity Precautions

Patients should avoid activities that put the implanted system under extreme stress.

- Avoid rubbing the Stimulator through the skin and activities that require excessive or repetitive twisting, bending, bouncing or stretching. These activities can damage the implanted system resulting in loss of symptom relief and additional surgery. Examples of activities to avoid are gymnastics, mountain biking, sky diving, skiing, and other sports. Less extreme activities should not impact your system, like running, jogging, road biking, swimming, and sexual activity.
- Scuba diving below 10 meters (33 feet) of water or entering hyperbaric chambers above 200kPa should be avoided.
- A perceived increase in stimulation may be caused by electromagnetic interference, postural changes, and other activities. You may find this uncomfortable (a jolting or shocking feeling). Before engaging in activities that receiving a jolt would be unsafe for you or those around you, lower the stimulation amplitude to the lowest setting and turn off the Neurostimulator.

Consult your doctor if you have any questions or concerns about physical activities.
Medical Procedure Precautions

Some medical procedures could adversely affect you and your Axonics SNM System.

Talk to your doctor about your Axonics SNM System before having any medical procedure.

Magnetic Resonance Imaging (MRI)
The Axonics SNM System is an MRI Conditional system. Refer to “MRI Patient Guidelines for the Axonics SNM System” for more information.

Diathermy
Shortwave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (collectively described as diathermy) CANNOT be performed if you have an implanted Axonics SNM System. Diathermy can transmit energy through the implanted system, potentially causing tissue damage at the location of the implanted electrodes, resulting in severe injury.

Other Medical Procedures
Additional medical procedures that may affect your Axonics SNM System and should be avoided include:

- Lithotripsy
- Monopolar electro-surgery
- Microwave and Radio-frequency (RF) ablation
- Radiation therapy over the Neurostimulator
- Ultrasound or scanning equipment
Living with the Axonics SNM System

Effects on Other Implanted Devices

The effect of the Axonics SNM System on the operation of other implanted devices, such as cardiac devices, other Neurostimulators, and implantable drug pumps, is not known. In particular, if the Axonics device is implanted close to one of these devices, they may have sensing problems and/or inappropriate device responses. Potential interference issues should be investigated before surgery by clinicians involved with both devices. The programming of the devices may need to be optimized to provide maximum benefit from both devices.

Neurostimulator Interaction with Implanted Cardiac Devices

When a patient needs both an Axonics SNM System and an implanted cardiac device (for example, a pacemaker or defibrillator), interactions between the two devices should be discussed by the patients’ physicians involved with both devices (such as the cardiologist, electrophysiologist, urologist, and urogynecologist) before surgery. To reduce potential interference, the devices should be implanted on opposite sides of the body and as far away from each other as practical.

The stimulation pulses produced by the Axonics SNM System may interact with cardiac devices that sense cardiac activity, leading to inappropriate behavior of the cardiac device.
Living with the Axonics SNM System

EMI Precautions

Energy from equipment found at home, work, or in public can potentially interfere with the Axonics SNM System. This is called electromagnetic interference (EMI). The Axonics SNM System has features that protect from EMI. Most electrical devices will not affect the Stimulator. Keep your distance from powerful electrical items to reduce the risk of potential problems.

Everyday electrical devices are not likely to affect your Stimulator. There are strong sources of EMI that have a higher risk. These include, anti-theft detectors found in stores to detect stolen merchandise. If you encounter any such devices, walk far away from the sides of the device when passing through. Some anti-theft detectors may not be visible. If you feel poorly, walk away from that area.

Airport security systems should not cause any interference problems with your Stimulator. Airport authorities advise patients to carry their Patient ID Card with them when traveling. They advise you to walk through metal detectors normally. Handheld security wands should move over stimulator quickly. Full-Body Scanners (millimeter wave scanners) are considered safe with implants by Transportation Security Administration (TSA). However, you should not linger within the detection zone.

You may encounter additional equipment that generates EMI. This equipment is unlikely to affect the Axonics SNM System if you follow these guidelines:
Living with the Axonics SNM System

**Bone growth stimulators** – The external coils of bone growth stimulators should be kept at least 45 cm (18 in) away from the Axonics SNM System. Do not use a bone growth stimulator if it is not working as intended.

**Dental drills and ultrasonic probes** – The drill or probe should be kept 15 cm (6 in) away from the Neurostimulator. The Neurostimulator should be turned off.

**Electrolysis** – The electrolysis wand should be kept at least 15 cm (6 in) away from the Neurostimulator. The Neurostimulator should be turned off.

**Electromagnetic field devices** – The following equipment or environments should be avoided or you should exercise caution around:

- Antenna of citizens band (CB) radio or ham radio
- Electric arc welding equipment
- Electric induction heaters such as those used in industry to bend plastic
- Electric steel furnaces
- High-power amateur transmitters
- High-voltage areas (generally safe if outside the fenced area)
- Linear power amplifiers
- Magnetic degaussing equipment
- Magnets or other equipment that generates strong magnetic fields
- Microwave communication transmitters (generally safe if outside the fenced area)
- Perfusion systems
- Resistance welders
- Television and radio transmitting towers (generally safe if outside the fenced area)
Living with the Axonics SNM System

**Laser procedures** – The laser should not be directed at the Neurostimulator. The Neurostimulator should be turned off.

**Psychotherapeutic procedures** – Equipment used for psychotherapeutic procedures may induce electrical currents which may cause heating at the lead electrodes and could result in tissue damage. Equipment that generates electromagnetic interference (e.g., electroconvulsive therapy, transcranial magnetic stimulation) during psychotherapeutic procedures have not been established as safe to operate in a patient with a Neurostimulator. Induced electrical currents may cause heating, especially at the lead electrode site, resulting in tissue damage.

**Radiation therapy** – Neurostimulator operation may be affected by high-radiation exposure. Sources of high-radiation should not be directed at the Neurostimulator. Neurostimulator damage due to high-radiation exposure may not be immediately evident, and exposure should be limited using appropriate measures, including shielding and adjusting the beam angle to avoid exposure to the Neurostimulator.

**Transcutaneous electrical nerve stimulation (TENS)** – TENS electrodes should not be placed in locations where the TENS current passes over any component of the Axonics SNM System. Discontinue using TENS if it starts affecting the performance of the Axonics SNM System.

If you think that an EMI generating equipment or environment is affecting the function of their Axonics SNM System, you should:
Living with the Axonics SNM System

1. Move away from the equipment or object.
2. Turn off the equipment or object. (if possible)
3. Use the patient Remote Control to adjust stimulation if necessary and to confirm the system is functioning appropriately.

If you are unable to eliminate the interference or believe the interference has altered the effectiveness of your therapy, you should contact your clinician.

Sources of strong EMI can result in the following:

- **Serious patient injury**, resulting from heating of the Neurostimulator and/or leads that causes damage to surrounding tissue.

- **System damage**, which may require surgical replacement due to change in symptom control.

- **Operational changes to the Neurostimulator**, causing it to turn on or off or to reset the settings, resulting in loss of stimulation or return of symptoms, causing a need for reprogramming by the clinician.

- **Unexpected changes in stimulation**, leading to a sudden increase or change in stimulation, which may be experienced as a jolting or shocking sensation. While the sensation may be uncomfortable, the device would not be damaged nor would it cause direct injury to the patient. In rare cases, the change in stimulation may cause the patient to fall and be injured.
Risks and Complications

A list of a potentially increased risks to sacral neuromodulation systems, including the Axonics SNM, is provided below:

- Adverse reaction to device materials
- Infection
- Device fracture/failure
- Electrical Shock
- Change in stimulation
- Lack of effectiveness
- Reoperation/Revision
- Seroma
- Device migration
- Complications usually associated with neuromodulation system implantation and use, include:
  - Adverse change in voiding function (bowel and/or bladder)
  - Change in sensation or magnitude of stimulation which has been described as uncomfortable (jolting or shocking) by some patients
  - Pain/Irritation
  - Undesirable change in pelvic function
  - Bleeding, including hematoma
  - Nerve injury
  - Soft tissue damage
Introduction

The Axonics SNM System includes a Remote Control that you should carry with you at all times. You can monitor your Stimulator using the Remote Control.

You should not need the Remote Control to change your stimulation. Your doctor should set your stimulation settings.

Your doctor will train you to use your Remote Control. A summary of how to use the Remote Control is on the following pages.

*Note: Bring your Remote Control to all your doctor visits.*
Recommended Use and Care

- Carry your Remote Control with you at all times in case you need to adjust stimulation or check the battery status of your Stimulator.

- To avoid damaging the Remote Control, do not drop it in liquid or clean it with harsh cleaners. You can clean the Remote Control with damp, soft cloth as needed.

- Avoid placing the Remote Control over or near other active implanted medical devices (for example pacemaker, defibrillator and other neurostimulators)

- Do not use the Remote Control near flammable or explosive gases.
Using Your Remote Control

Buttons and Lights

**Stimulation Level** – Shows the strength of stimulation

- **Up** – Turn up stimulation level or Turn on stimulation to default level

- **Connect** – Connect or disconnect the Patient Remote to the Stimulator

- **Down** – Turn down stimulation level or Turn off stimulation

- **System Error** – Shows there is an error in the Remote Control or Stimulator

**Stimulator Battery Status** – Shows if the battery needs charging

**Active Program** – Not applicable
Connecting to the Stimulator

To use your Remote Control, follow these steps to connect to the Stimulator:

1. Hold the Remote Control comfortably in front of you on the same side of your body as your Stimulator.

2. Press the “Connect” button on the center of the Remote Control.

3. The stimulation level lights will flash. Flashing means the Remote Control is trying to connect to the Stimulator. It may take up to 12 seconds for the Remote Control to start communicating with the Stimulator.

4. Watch for the stimulation level lights to stop flashing and the Stimulator battery light to turn on. This means the Remote Control is communicating with the Stimulator. If no lights are on, the connection failed. Move the Remote Control closer to where the Stimulator is implanted and try again.

Note: Moving the Patient Remote while it is connected to the Stimulator may result in disconnection.
Reading the Lights

**Stimulator Battery Status**
- Solid Green: Stimulator battery will last for 4 or more days
- Flashing Green: Stimulator battery is charging
- Solid Orange: Stimulator battery will last for 2 to 4 days
- Flashing Orange: Stimulator battery will last for 2 days or less

**Stimulation Level Indicators**
- No stimulation
- Default level set by your doctor
- Maximum level
Monitoring Stimulation Status

System Error light

When you try to connect to your Stimulator, the Remote Control will check for errors. Call your doctor when the red error light is on.

Red light flashes – Ask for a new Remote Control.

Red light is on at all times – The doctor needs to test your Stimulator. Make an appointment to see your doctor.

*Note:* The Remote Control is not serviceable. It must be returned to Axonics for replacement.
Changing Stimulation

You should feel stimulation at all times, and if you do not feel the stimulation you should increase the stimulation strength. If you need to change your stimulation, you can use your Remote Control to turn up or down the stimulation or completely turn off the stimulation.

Turn Up Stimulation
Press + Release: Turn up stimulation strength by one level
Press + Hold for 5 seconds: Turn stimulation on (if stimulation is off)

Turn Down Stimulation
Press + Release: Turn down stimulation strength by one level
Press + Hold for 5 seconds: Turn stimulation off

Note: The Remote Control will vibrate when a command has been successfully received by the Stimulator. A change in the stimulation level lights will also occur.
The Axonics SNM System includes a small rechargeable Stimulator that will typically need to be recharged every one (1) or two (2) weeks.

How often you need to charge will depend on the stimulation level settings of the Stimulator. When your doctor programs your Stimulator, they will tell you how often you should charge. You can check your battery status using your Remote Control so you know when to charge.

To charge, you place the Charger on your skin over the Stimulator implant site. The Charger passes energy through the skin to charge the Stimulator battery. The amount of time it will take to charge the battery will depend on how low the Stimulator battery is. This usually should not take more than two hours.
Introduction

The Axonics Charging System allows you to customize how you charge:

- Determine how often you want to charge - charge more often for shorter charge times
- Select from 2 options for holding your Charger in place during charging – you can use the carrier or the charge belt
- Pick your preferred activity for while you charge – you can perform basic activities while charging

The Axonics SNM System provides sound, vibration, and visual feedback to help you charge your Stimulator.

Detailed instructions on using your Charger will be given by your doctor and his or her staff. A summary is on the following pages.

Note: The rechargeable Neurostimulator battery should provide 15 or more years of service. With repeated charging the battery may lose capacity and require recharging more often. Notify your doctor if you experience a change in the life of your rechargeable Neurostimulator battery that requires charging more than twice as often as when initially programmed. For example, notify your doctor if your fully charged Stimulator battery initially lasted 2 weeks and after several years only lasts for 1 week.

Note: Do not lie on your charger or wear heavy clothing or a blanket over the charger as this could cause heat to build up around the charger.
Charging Your Stimulator

Charging-System Components

**Charger**
*Charges the Stimulator*

**Carrier**
*Holds the Charger in place during charging*

**Charge Belt**
*Holds the Charger in place during charging*

**Dock**
*Stores and charges the Charger*

**Power Supply**
*Connects the Dock to a power source*
Get the Charger Ready

1. Remove the Charger from the Dock
   Note: A green light on the Charger means it has enough power to fully charge the Stimulator

2. Snap the Charger on the Carrier (shown below) or the Charge Belt. If you use the Carrier, remove the plastic liner to expose the adhesive patches
Align the Charger with the Stimulator

For best charging, place the Charger over your implanted Stimulator. You should place your Charger with the button facing up if your Stimulator is placed horizontally (as shown to the right). Your doctor will inform you if your Stimulator is placed in a different way.

To place the Charger, hold the Charger over your Stimulator. Slowly move the Charger in that area until you hear one long tone. This indicates the Charger is properly aligned and is charging the Stimulator. When you hear the long tone, press the carrier adhesives onto your skin or strap the belt tightly in place.
Monitor Your Charging

During charging you can monitor charging by observing the following indicators:

<table>
<thead>
<tr>
<th>Recharge Status</th>
<th>Feedback</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Stimulator is charging</td>
<td>Flashing green lights on Charger and Remote Control</td>
</tr>
<tr>
<td>Charging has been interrupted</td>
<td>Three beeps and vibration (repeats every 5 seconds)</td>
</tr>
<tr>
<td>Charging has been completed</td>
<td>Rising tone (repeats 3 times). + Charger and Remote Control lights stop flashing</td>
</tr>
</tbody>
</table>

If your charging is interrupted realign the Charger with the Stimulator to resume charging.
Completing Charging

When you have completed charging the Stimulator:

1. Remove the Charger and the carrier or charge belt
   a) Dispose of the carrier in the trash
   b) Store the charge belt until the next charging
2. Place the Charger on the Dock to ensure it has enough power next time you charge your Stimulator

*Note: The Charging System is not serviceable. If you experience an issue, the Charging System must be returned to Axonics for replacement.*
Device Disposal

To dispose of any component of your system, it is recommended to return the component back to your doctor.

Do not throw the components in the regular trash. Follow your local government rules to dispose of any component, particularly components with batteries.

Do not throw any components with batteries (or the batteries themselves) in fire as the battery may explode.
Introduction

This section will help you solve issues with your Axonics SNM System. If you experience issues with your therapy, using your Remote Control, or using the Charging System, please see if the following troubleshooting steps might resolve your issue.

Contact your doctor or Axonics Customer Support if you need help resolving your issue, including for issues not included in this section.
# Remote Control Troubleshooting

<table>
<thead>
<tr>
<th>Issue</th>
<th>Presentation</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remote Control will not connect to Stimulator</td>
<td>Remote Control lights scroll then go off. Battery Status indicator is not lit.</td>
<td>Move Remote Control closer to Stimulator and retry connection. Next try charging the Stimulator. If issue persists, contact your doctor.</td>
</tr>
<tr>
<td>Remote Control will not connect to Stimulator</td>
<td>Remote Control does not respond when “Connect” button is pressed</td>
<td>Contact your doctor for a new Remote Control</td>
</tr>
<tr>
<td>Error indicator is visible on the Remote Control</td>
<td>Red error light flashes for 12 seconds then is off</td>
<td>Disconnect Remote Control from Stimulator; Press “Up” and “Down” buttons to check if they are stuck; Reconnect to Stimulator. If issue persists, contact your doctor</td>
</tr>
<tr>
<td>Error indicator is visible on the Remote Control</td>
<td>Red error indicator is on</td>
<td>Contact your doctor</td>
</tr>
<tr>
<td>Unable to adjust stimulation</td>
<td>Remote Control connects to Stimulator but stimulation cannot be turned up or turned down</td>
<td>Contact your doctor</td>
</tr>
<tr>
<td>Unable to adjust stimulation</td>
<td>Remote Control lights are scrolling or Remote Control lights are not illuminated</td>
<td>Reconnect and retry adjustment. Contact your doctor</td>
</tr>
<tr>
<td>Damage to Remote Control</td>
<td>Remote Control appears physically damaged</td>
<td>Stop use of the Remote Control. Contact your doctor to discuss replacement</td>
</tr>
<tr>
<td>Discomfort or pain due to stimulation</td>
<td>Constant pain or discomfort in the groin or buttocks</td>
<td>Turn down stimulation level. If issue persists, turn off stimulation and contact your doctor</td>
</tr>
<tr>
<td>Remote Control will not turn off</td>
<td>Light(s) will not turn off</td>
<td>Retry turning the Remote Control off (press “Connect” button). Contact your doctor for replacement.</td>
</tr>
</tbody>
</table>
## Charging Troubleshooting

<table>
<thead>
<tr>
<th>Issue</th>
<th>Presentation</th>
<th>Resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Charger is not charging the Stimulator</td>
<td>The power light on the Charger is green. Nothing happens when you place the Charger over the Stimulator.</td>
<td>Retry placing the Charger, making sure the Charger is placed the correct way over your Stimulator (see “Where to Place the Charger”). If you still cannot charge, contact your doctor.</td>
</tr>
<tr>
<td>Charger is not charging the Stimulator</td>
<td>The power light on the Charger is blank and does not turn on when you press the power button.</td>
<td>Place the Charger on the Dock to charge the Charger. Retry charging when the Charger light is solid green.</td>
</tr>
<tr>
<td>Charger is not charging the Stimulator</td>
<td>Charging stopped. Three beeps are heard and the Charger vibrated.</td>
<td>Check the Charger power level. If “green”, place the Charger over the Stimulator again. If charging does not start, contact your doctor.</td>
</tr>
<tr>
<td>Dock will not charge the Charger</td>
<td>Charger is placed in Dock and the power light does not come on.</td>
<td>Check to make sure the Dock is plugged in to an outlet using the power supply. Next, pick up and put the Charger back in the Dock. Make sure it is lined up with the Dock correctly. If you still cannot charge the Charger, contact your doctor.</td>
</tr>
<tr>
<td>Dock will not charge the Charger</td>
<td>Charger is placed in Dock and red error light comes on.</td>
<td>There is an error in charging the Charger. Turn the Charger off then back on. If the red light is still on, contact your doctor.</td>
</tr>
<tr>
<td>Damage to the Charger</td>
<td>Charger has visible damage.</td>
<td>Do not use your charger. Contact your doctor to discuss replacement.</td>
</tr>
<tr>
<td>Stimulator has to be charged more often</td>
<td>Over time, the Stimulator battery provides 50% less stimulation time between charges than it did after initial programming.</td>
<td>If stimulation settings were changed recently, the change in charging frequency is expected. If stimulation settings were not changed, contact your doctor to discuss the change in your Stimulator battery life.</td>
</tr>
<tr>
<td>Error light is on</td>
<td>The Charger shows a red light when it is turned on.</td>
<td>There is an error in the Charger. Turn the Charger off then back on. If the red light is still on, contact your doctor.</td>
</tr>
</tbody>
</table>
System Specifications

Stimulation Output

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency</td>
<td>2 – 130 Hz</td>
</tr>
<tr>
<td>Pulse Width</td>
<td>60 – 450 us</td>
</tr>
<tr>
<td>Amplitude</td>
<td>0 – 12.5 mA</td>
</tr>
</tbody>
</table>

Additional technical information is available. Please contact Axonics if you want to request additional information.

Wireless Communication

This device complies with part 15 of the FCC Rules. Operation is subject to the following two conditions:
(1) This device may not cause harmful interference, and
(2) This device must accept any interference received, including interference that may cause undesired operation.

This transmitter is authorized by rule under the Medical Device Radio communication Service (in part 95 of the FCC Rules) and must not cause harmful interference to stations operating in the 400.150–406.000 MHz band in the Meteorological Aids (i.e., transmitters and receivers used to communicate weather data), the Meteorological Satellite, or the Earth Exploration Satellite Services and must accept interference that may be caused by such stations, including interference that may cause undesired operation.

This transmitter shall be used only in accordance with the FCC Rules governing the Medical Device Radio communication Service. Analog and digital voice communications are prohibited.
Although this transmitter has been approved by the Federal Communications Commission, there is no guarantee that it will not receive interference or that any particular transmission from this transmitter will be free from interference.

**Note:** Changes and modifications to the system not authorized by Axonics could void FCC and IC certification and negate the user’s authority to use the product.

**Quality of Wireless Service:** This device operates in the 401-406 MHz frequency and the maximum effective radiated power of the Neurostimulator communication is below the limit of 25 μW ERP/EIRP as specified in EU: EN ETSI 301-839 and USA: FCC 47 CFR Part 95; Subpart I. The Remote Control, Clinician Programmer, or Charger have to be within 1 meter from the Neurostimulator or Trial Stimulator for successful communication.

**Wireless Security:** The Neurostimulator or Trial Stimulator can only communicate with a single Remote Control that is paired to it using the Clinician Programmer. Any Axonics Clinician Programmer or Charger can communicate with a Neurostimulator. Additional mechanisms exist to ensure the integrity of radio data.
EC REP
HealthLink Europe Services BV
De Tweeling 20-22
5215 MC 's-Hertogenbosch
The Netherlands

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Axonics Modulation Technologies, Inc.
110-0047-001 DRAFT 11