Sacral Neuromodulation System

Neurostimulator Implant Manual

Model 1101 Neurostimulator

Rx only

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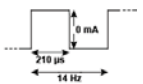
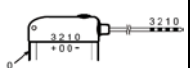
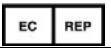
LABEL SYMBOLS

This section explains the symbols found on the product and packaging.

Symbol	Description
	Axonics Neurostimulator
	Axonics Torque Wrench
	Neurostimulator default waveform with 14 Hz frequency, 0 mA amplitude and 210 µs pulse width
	Neurostimulator default electrode configuration: Electrode 0: negative (-) Electrode 1: Off (0) Electrode 2: Off (0) Electrode 3: Positive (+) Case: Off (0)
	Product Serial Number
	Manufacturer
	Product Model Number

Symbol	Description
	Manufacturing Date
	Non ionizing electromagnetic radiation
CE 2797	Conformité Européenne (European Conformity). This symbol means that the device fully complies with AIMD Directive 90/385/EEC (Notified Body reviewed) and RED 2014/53/EU (self-certified)
	Refer to instructions for use (Consult accompanying documents)
	Temperature limitation
	Humidity limitation
	Pressure limitation
	Do not reuse
STERILE EO	Sterilized using Ethylene oxide
	Use by
	Do not use if package is damaged
	Do not re-sterilize

Symbol	Description
	Authorized representative in the European community
	Open here
	For USA audiences only Caution: U.S. Federal law restricts this device for sale by or on the order of a physician
	Warning / Caution
	Product Literature
	Magnetic Resonance (MR) Conditional
IC	Industry Canada certification number
	This device complies with all applicable Australian Communications and Media Authority (ACMA) regulatory arrangements and electrical equipment safety requirements
FCC ID	US Federal Communications Commission device identification

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INTRODUCTION

This manual provides information about the Axonics Sacral Neuromodulation (SNM) System Neurostimulator (Model 1101), which is a part of the Axonics SNM System. The Neurostimulator is connected to the Axonics tined lead (Model 1201 or 2201).

DEVICE DESCRIPTION

The Axonics Neurostimulator (**Figure** 1) is part of the Axonics SNM System. The Neurostimulator is a programmable device that is connected to the Axonics tined lead, which conducts stimulation pulses to the sacral nerve.

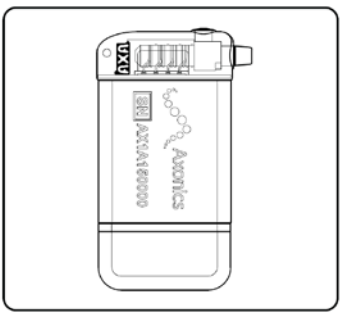

Figure 1: Axonics Neurostimulator.

Package contents

The **Neurostimulator** package contains the following:

- Neurostimulator
- Torque wrench
- System registration form
- Patient identification card
- Neurostimulator Implant Manual (this document)

The contents of the inner package are STERILE. The contents of the Neurostimulator package are intended for single use only.

System registration form and Patient identification card

The system registration form registers the device and creates a record of the device in Axonics' implant data system.

The patient identification card is also packaged with this device. The patient should carry the identification card at all times.

AXONICS SNM THERAPY FOR URINARY CONTROL

Indications

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.

Warning: This therapy is not intended for patients with mechanical obstruction such as benign prostatic hypertrophy, cancer, or urethral stricture.

Contraindications

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

WARNINGS

Prohibited Medical Procedure

Diathermy

Shortwave diathermy, microwave diathermy, or therapeutic ultrasound diathermy (collectively described as diathermy) CANNOT be performed on patients implanted with the 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 Guidelines for the Axonics Sacral Neuromodulation System" for more information.

Other Medical Procedures

Additional medical procedures that may adversely affect the patient or the 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.

Case Damage

The Neurostimulator contains battery chemicals that could cause severe burns if the Neurostimulator case were ruptured or pierced.

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**.**

Charging Use

If swelling or redness occurs near the Charger attachment site, the patient should contact their clinician before using the Charger again. Swelling or redness may indicate an infection or an allergic reaction to the Charger adhesive.

PRECAUTIONS

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.

Clinician Programming

Parameter Adjustment – The steps below should be taken to prevent sudden stimulation changes that lead to an uncomfortable jolting or shocking feeling:

- Stimulation parameters should be changed in small increments.
- The stimulation amplitude should be allowed to ramp to full amplitude slowly.
- Before disconnecting the stimulation cable or turning the simulation on or off, the stimulation amplitude should be decreased to 0.0 mA.

Sensitivity to Stimulation – Some patients, especially those that are very sensitive to stimulation, may be able to sense

the telemetry signals associated with reprogramming.

Programmer Interaction with a Cochlear Implant – Patients with cochlear implants should keep the external portion of their cochlear implant as far from the Clinician Programmer (CP) or Remote Control as possible to minimize unintended audible clicks or other sounds.

Programmer Interaction with Flammable Atmospheres – The CP is not intended to be used in the presence of a flammable gas, and the consequences of using the CP in such an environment is not known.

Programmer Interaction with Other Active Implanted Devices – When a patient has a Neurostimulator and another active implanted device (for example, a pacemaker, defibrillator, or another neurostimulator), the RF signal used to program any of these devices may reset or reprogram the other devices.

Whenever the settings for these devices are changed, a clinician familiar with each device should check the program settings of each device before the patient is released (or as soon as possible). Patients should contact their physician immediately if they experience symptoms that are likely to be related to the devices or their medical condition.

Telemetry Signal Disruption from EMI – The Neurostimulator should not be programmed near equipment that may generate electromagnetic interference (EMI) as the equipment may interfere with the CP or Remote Control's ability to communicate with the Neurostimulator. If EMI is suspected to be interrupting programming, the CP or Remote Control and the Neurostimulator should be moved away from the likely source of EMI.

Electromagnetic Interference (EMI)

Patients may encounter additional equipment that generates EMI. This equipment is unlikely to affect the Axonics SNM System if the patients follows these guidelines:

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 patients 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)

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 a patient thinks that an EMI generating equipment or environment is affecting the function of their Axonics SNM System, the patient should:
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 the patient is unable to eliminate the interference or believes the interference has altered the effectiveness of their therapy, the patient should contact their clinician.

- **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.

Patient Activities

Activities Requiring Excessive Twisting or Stretching – Patient activities that may strain the implanted components of the Axonics SNM System should be avoided. For example, movements that include sudden, excessive, or repetitive bending, twisting, bouncing, or stretching may cause migration or breakage of the Axonics SNM leads. Lead breakage or migration may cause loss of stimulation, intermittent stimulation, or stimulation at the fracture site. Additional surgery may be required to replace or reposition the component. Activities that typically involve these movements include gymnastics, mountain biking, and other vigorous sports. Clinicians should ask their patients about the activities in which they participate and inform them of the need for restricted activities.

Component Manipulation by Patient (Twiddler's Syndrome) – Clinicians should advise patients to refrain from manipulating the Axonics SNM System through the skin. Manipulation may cause device damage, lead migration, skin erosion, or uncomfortable stimulation.

Scuba Diving or Hyperbaric Chambers – Pressures below 10 meters (33 feet) of water (or above 200 kPa) could damage the Axonics SNM System. Diving below 10 meters (33 feet) of water or entering hyperbaric chambers above 200 kPa should be avoided. Patients should discuss the effects of high pressure with their physician before diving or using a hyperbaric chamber.

Skydiving, Skiing, or Hiking in the Mountains – High altitudes should not affect the Neurostimulator. Nevertheless, patients should be cautious with high altitude activities due to the potential for movements that may put stress on the implanted components. For example, the sudden jerk that occurs when a parachute opens while skydiving may cause lead breakage or migration, which may require surgery to replace or remove the lead.

Unexpected Changes in Stimulation – A perceived increase in stimulation may be caused by electromagnetic interference, postural changes, and other activities. Some patients may find this uncomfortable (a jolting or shocking feeling). Before engaging in activities that receiving a jolt would be unsafe for the patient or those around them, patients should lower the stimulation amplitude to the lowest setting and turn off the Neurostimulator. Patients should also discuss these activities with their clinician.

Patient Programming and Remote Control

Patient Access to Remote Control – Patients should carry their Remote Control with them at all times to allow them to adjust the stimulation amplitude and/or turn on/off the Neurostimulator.

Remote Control May Affect Other Implanted Devices – Patients should avoid placing the Remote Control over or near other active implanted medical devices (for example pacemaker, defibrillator and other neurostimulators).

Remote Control Handling – To avoid damaging the Remote Control, patients should avoid immersing it in liquid and should clean it with damp soft cloth. Patients should avoid dropping the device or mishandling it in any way that may damage it.

Remote Control Use – Patients should avoid operating the Remote Control when near flammable or explosive gases.

Storage and Usage Environment

Component Packaging – Any component that has been compromised in any way should not be implanted. Do not implant the component if any of the following have occurred:

- The storage package or sterile pack has been damaged, pierced, or altered, as sterility cannot be guaranteed, which may lead to infection.
- The component itself shows any signs of damage. The component may not function properly.
- The use-by date has expired. In this case, component sterility cannot be guaranteed and infection may occur.

- The sterile component was dropped onto a non-sterile surface. In this case, the sterility cannot be guaranteed and infection may occur.

Usage Environment:

The following lists the appropriate temperature, humidity, and pressure usage conditions for use of the Neurostimulator:

- Temperature: 20 °C to 45 °C
- Pressure: The Neurostimulator should function at up to 10 m (33 feet) underwater (200 kPa) and at altitudes up to 3000 m (10,000 feet) associated with activities like hiking and skydiving (as low as 70 kPa)

Shipping and Storage Environment:

The following lists the appropriate temperature, humidity, and pressure conditions for shipping and storing the Neurostimulator:

- Temperature (short term: 3 days): -10 °C to 55 °C
- Temperature (long term): 20 °C to 30 °C
- Humidity (short term: 3 days): 15% to 95%
- Humidity (long term): 30% to 85%
- Pressure (short term): 57 kPa to 106 kPa
- Pressure (long term): 70 kPa to 106 kPa

If the Neurostimulator is exposed to extreme temperatures, it may be permanently damaged and should not be used, even if it has returned to a temperature that is within the specified operating range.

Sterilization

The contents of this package have been sterilized using

ethylene oxide. This device is for single use only and should not be re-sterilized.

System Implant

Compatibility – For proper therapy, use only Axonics SNM components. The use of non-Axonics components with the Axonics SNM System may result in damage to Axonics components, loss of stimulation, or patient injury. Use of non-Axonics components voids Axonics warranty coverage.

Component Failures – The components of the Axonics SNM System may fail at any time. Such failures, such as electrical shorts, open circuits, and insulation breaches are unpredictable. Also, the Neurostimulator battery will eventually fail to recharge. The rechargeable Neurostimulator battery should provide at least 15 years of service and with repeated charging the battery will lose its ability to recharge to its full capacity. This may result in the Neurostimulator requiring more frequent recharging. When stimulator can no longer be maintained with regular charging, the Neurostimulator may need to be replaced.

Component Handling – The components of the Axonics SNM System must be handled with extreme care. They may be damaged by excessive force or sharp instruments, which can lead to intermittent stimulation or loss of stimulation altogether and may require surgery to replace. Do not use saline or other ionic fluids at connections, which could result in a short circuit.

POTENTIAL ADVERSE EVENTS SUMMARY

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
- Infection
- Pain or irritation at Neurostimulator and/or lead site
- 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
- Heating or burn at Neurostimulator site
- Lack of effectiveness
- Reoperation/Revision
- Undesirable change in pelvic function

INDIVIDUALIZATION OF TREATMENT

The patient should be fully informed about the risks and benefits of SNM therapy, including risks of the surgical procedure, follow-up responsibilities, and self-care requirements. In order to achieve optimal benefits from the therapy, the Axonics SNM System requires a long-term commitment to post-surgical management.

Patient Selection – Patients should be carefully selected to ensure they meet the following criteria:

- The patient is an appropriate surgical candidate with special consideration for the lead length, implant depth, and ability to successfully implant the lead and route the lead to the Neurostimulator.
- The patient can properly operate the Axonics SNM System, including the ability to use the Remote Control, to detect alignment of the Charger, and to understand when charging is complete.
- Trial Stimulation: The patient has undergone a trial stimulation with either a temporary lead for up to 7 days, or a permanent lead for up to 14 days, and he/she experienced a 50% reduction in urinary symptoms.
- The patient does not have a history of sensitivity to stimulation.

SUMMARY OF CLINICAL EVALUATION

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."[2]

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 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 efficacy 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[7], and Siegel 2018[9]), 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[3] and Siddiqui 2008[6]) and five original clinical research articles (Amundsen 2018[1], Siegel 2015, Siegel 2018, White 2009[12], van Kerrebroeck 2007[11]). 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.

Table 2: Adverse Events Reported in the Literature for the InterStim System.

Article Reference	Follow up duration	Adverse Events	SAE
Amundsen 2018[1] (139 subjects)	2 years	• Device revision 3% • Device removal 8.6% • Infection 2.9% • Pain 1.4% • Procedural pain 6.0%	• NR ŧ
Herbison 2009[3]* (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 ŧ
Siddiqui 2010[6]*** (Spinelli 2005: 127 subjects)	13.8 months	• Lead migration 7% • Lead revision performed 3%	• NR ŧ
Siegel 2015[7] € (InSite study – Phase 1) (59	6 months	• Change in stimulation, undesirable 10.2% • Pain, implant site 8.5% • Lead migration/dislodgement 3.4%	• 0%

Article Reference	Follow up duration	Adverse Events	SAE
subjects with test stimulation, 51 subjects with full system implant)		• Infection, implant site 3.4% • Surgical intervention† 3.9%	
Siegel 2018[9] (InSite study – Phase 2) (272 subjects)	5 years	• Surgical intervention related to tined lead 22.4% (primary safety endpoint) • Undesirable change in stimulation 22% • Implant site pain 15% • Therapeutic product ineffective 13% • Implant site erosion 0.4% • Other AEs 6% • Surgical interventions **** o Due to AE 30.9% o Due to Battery replacement 33.5% o Due to lack or loss of effectiveness 33.5% o Permanent explant 19.1%	• Implant site erosion 0.4% §

Article Reference	Follow up duration	Adverse Events	SAE
van Kerrebroeck 2007[11] ¥ (152 subjects)	5 years	• New pain/undesirable change in stimulation 28.3% • Pain at neurostimulator site 19.8% • Pain at lead site 7.9% • Infection at lead or neurostimulator site 7.9% • Sensation of electric shock** 7.9% • Undesirable change in voiding function 7.2% • Lead migration 8.6% • Technical problems during implant (surgery) 5.3% • Device problem 10.6% • Other AE 33.6% • Surgical intervention 39.5% • Device explant 10.5% • Device exchange 23.7%	• NR ŧ
White 2009[12] € (221 subjects with test stimulation, 202	36.9 months	• Pain, implant site 2.9% • Device malfunction, secondary to trauma 8.9% • Infection 3.5%	• NR ŧ

Article Reference	Follow up duration	Adverse Events	SAE
subjects with full system implant)		• Post-operative hematoma requiring intervention 1.5% • Lead migration 5.9% • Explant due to lack of effectiveness 3.5% • Revision due to battery depletion 2% • Elective removal 5% • Overall surgical intervention 30.3%	

Ł 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; 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

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 AE. 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 AE 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 efficacy, four subjects (2.0%) required revision secondary to battery expiration, and 10 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' 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.

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 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 3: Device Related AEs and SAEs Reported in the ARTISAN-SNM Study.

	Device Related			Serious Device Related		
AE Type	**Events (n)**	**Subjects (n/N) (%)**	**Events (Subjects)**	**Events (n)**	**Subjects (n/N) (%)**	**Events (Subjects)**
Proctalgia	1	1 (0.8)	1 (1)	0	0 (0.0)	0 (0)
Pain	1	1 (0.8)	1 (1)	0	0 (0.0)	0 (0)
Medical device discomfort	1	1 (0.8)	1 (1)	0	0 (0.0)	0 (0)
Implant site pain	2	2 (1.6)	2 (2)	0	0 (0.0)	0 (0)
Incision site infection	1	1 (0.8)	1 (1)	0	0 (0.0)	0 (0)
Pain at extremity	2	2 (1.6)	2 (2)	0	0 (0.0)	0 (0)
Groin Pain	1	1 (0.8)	1 (1)	0	0 (0.0)	0 (0)
Dysesthesia	1	1 (0.8)	1 (1)	0	0 (0.0)	0 (0)
Lead dislodgement	1	1 (0.8)	1 (1)	0	0 (0.0)	0 (0)
Vulvovaginal pain	1	1 (0.8)	1 (1)	0	0 (0.0)	0 (0)
Vulvovaginal discomfort	1	1 (0.8)	1 (1)	0	0 (0.0)	0 (0)
Total	**13**	**13 (10.1)**	**13 (13)**	**0**	**0 (0.0)**	**0 (0)**

Table 4: Procedure Related AEs and SAEs Reported in the ARTISAN-SNM Study.

	Procedure Related		Serious Procedure Related	
AE Type	**Events (n)**	**Subjects (n/N) (%)**	**Events (n)**	**Subjects (n/N) (%)**
Vomiting	1	1 (0.8)	0	0 (0.0)
Implant site pain	1	1 (0.8)	0	0 (0.0)
Hypersensitivity	1	1 (0.8)	0	0 (0.0)
Allergy to chemicals	1	1 (0.8)	0	0 (0.0)
Incision site infection	1	1 (0.8)	0	0 (0.0)
Fungal infection	1	1 (0.8)	0	0 (0.0)
Procedural pain	4	4 (3.1)	0	0 (0.0)
Incision site pain	1	1 (0.8)	0	0 (0.0)
Paraesthesia	1	1 (0.8)	0	0 (0.0)
Keloid scar	1	1 (0.8)	0	0 (0.0)
Dermatitis papillaris capillitii	1	1 (0.8)	0	0 (0.0)
Suture insertion	1	1 (0.8)	0	0 (0.0)
Total	**15**	**13 (10.1)**	**0**	**0 (0.0)**

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 5: Summary and time-course device-related adverse events

Number of implanted subjects = 129							
AE Type	**Implant to 2 Weeks**	**2 weeks to 1 Month**	**1 Month to 3 Months**	**3 Months to 6 Months**	**6 Months to 12 Months**	**Beyond 12 Months**	**Status Resolved*/ Ongoing**
Total events	***1***	***4***	***2***	***3***	***3***	***0***	***13/0***
Proctalgia	0	0	0	1	0	0	1/0
Pain	0	1	0	0	0	0	1/0
Medical device discomfort	0	0	0	0	1	0	1/0
Implant site pain	1	0	1	0	0	0	1*/0
Incision site infection	0	1	0	0	0	0	1/0
Pain in extremity	0	1	0	1	0	0	1/0
Groin pain	0	0	1	0	0	0	1/0
Dysaesthesia	0	0	0	0	1	0	1/0
Lead dislodgement	0	1	0	0	0	0	1/0
Vulvovaginal pain	0	0	0	0	1	0	1/0
Vulvovaginal discomfort	0	0	0	1	0	0	1/0

** Includes events that were resolved with sequelae*

Procedure-related adverse events

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

Number of implanted subjects = 129							
AE Type	**Implant to 2 Weeks**	**2 weeks to 1 Month**	**1 Month to 3 Months**	**3 Months to 6 Months**	**6 Months to 12 Months**	**Beyond 12 Months**	**Status Resolved */ Ongoing**
Total events	***10***	***3***	***1***	***1***	***0***	***0***	***13/2***
Vomiting	1	0	0	0	0	0	1/0
Implant site pain	1	0	0	0	0	0	1*/0
Hypersensitivity	0	1	0	0	0	0	1/0
Allergy to chemicals	1	0	0	0	0	0	1/0
Incision site infection	0	1	0	0	0	0	1/0
Fungal infection	0	1	0	0	0	0	1/0
Procedural pain	4	0	0	0	0	0	3/1
Incision site pain	1	0	0	0	0	0	1/0
Paraesthesia	0	0	1	0	0	0	0/1
Keloid scar	0	0	0	1	0	0	1*/0
Dermatitis papillaris capillitii	1	0	0	0	0	0	1*/0
Suture insertion	1	0	0	0	0	0	1/0

** Includes events that were resolved with sequelae*

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.

Article Reference	**# Subjects Receiving Test Stimulation**	**# Subjects Receiving Permanent Implant (% of subjects receiving test stimulation)**	**Follow up Duration with Permanent Implant** ***# subjects at follow up (% of subjects receiving permanent implant)***	**Effectiveness Endpoint (Responder Rate)**
Amundsen 2018	169 (UUI)	139 (82%)	2 years *122 subjects (88%)*	50%*
Herbison 2009**	NR	278 (NR)	NR	Details in Text
Siddiqui 2010***	NR	234 (OAB) (52-77%¥)	6 months-29 months	45% of subjects reported a lack of daily incontinence episodes

Article Reference	# Subjects Receiving Test Stimulation	# Subjects Receiving Permanent Implant (% of subjects receiving test stimulation)	Follow up Duration with Permanent Implant *# subjects at follow up (% of subjects receiving permanent implant)*	Effectiveness Endpoint (Responder Rate)
Siegel 2015 (InSite study – Phase 1)	59 (OAB) 29 (UUI) 19 (UF)	51 (86%)	6 months *51 subjects (100%)*	76% (OAB) 71% (UUI)[§] 61% (UF) Complete continence in 39% of UUI subjects
Siegel 2018 (InSite study – Phase 2)	340 (OAB) 202 (UUI) 189 (UF)	272 (80%)	5 years *150 (OAB) (55%)* 118 (UUI) 109 (UF)	82% (OAB) 76% (UUI)[§] 71% (UF) Complete continence in 45% of UUI subjects

Article Reference	# Subjects Receiving Test Stimulation	# Subjects Receiving Permanent Implant (% of subjects receiving test stimulation)	Follow up Duration with Permanent Implant *# subjects at follow up (% of subjects receiving permanent implant)*	Effectiveness Endpoint (Responder Rate)
van Kerrebroeck 2007	163 103 (UUI) 28 (UF) 31 (UR)	152 (93%) 96 (UUI) 23 (UF) 31 (UR)	5 years *105 subjects* (69%) *65 (UUI)* 27 (UF) 13 (UR)	58% (UUI)[§] 40% (UF)† 71% (UR)

**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 ≥ 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 ≥ 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 ≥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 ≥ 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 efficacy 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.

Table 7: Responder rate in all implanted subjects

Effectiveness Measure (N=129)	Responder Rate	Reject Null Hypothesis?	95% CI	P-value*
Responder rate in all implanted subjects at 6 months (As Treated)	89.9%	Yes	(83.4%, 94.5%)	<0.0001

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

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 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[4]; Siegel et al, 2016[8]).

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.

Table 8: Secondary effectiveness results in all implanted subjects

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

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 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 an overestimation of therapy results.

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PATIENT COUNSELING INFORMATION

Clinicians should provide the following:

- Information about the components of the Axonics SNM System.
- Instructions for using the Remote Control and Charging System.

Also, the clinician should provide each patient with a copy of the Axonics SNM System Patient Therapy Guide and, in particular, review the following sections with him/her:

- Getting the Axonics SNM System
- Living with the Axonics SNM System

Clinicians should also instruct their patients as follows:

- Patients should tell their healthcare professionals, including their primary doctor and dentist, that they have an implanted neuromodulation system. Patients should bring their Patient Therapy Guide to all medical and dental appointments in the event that their healthcare professional has any questions regarding any precautions to take to avoid potential device problems.
- Patients should always carry their Remote Control to allow them to change the stimulation amplitude and/or turn the Neurostimulator on or off.
- Patients should always bring their Remote Control to appointments related to their Axonics SNM System, including all programming sessions.
- Patients should contact their physician if they have any unusual signs or symptoms.

COMPONENT DISPOSAL

The following steps should be taken when the Axonics SNM System is explanted (for example, due to replacement, cessation of therapy, or after patient death) or when disposing of accessories:

- If possible, the explanted component should be returned to Axonics along with completed paperwork for analysis and disposal.
- The device should not be autoclaved or exposed to ultrasonic cleaners to allow it to be analyzed by Axonics.
- Any components not returned to Axonics should be disposed of according to local regulations. Any potentially contaminated materials should be treated as biohazardous waste.

Note that in some countries, explanting a battery-operated implantable device is mandatory.

Cautions:

- Components that are explanted or that have come into contact with bodily fluids should be handled with appropriate biohazard controls. Such components should only be returned to Axonics in packaging supplied by Axonics.
- The Neurostimulator may explode if subjected to high temperatures; therefore the Neurostimulator should not be incinerated and should be explanted before patient cremation.
- Implantable devices should not be reused after exposure to body tissues or fluids because the sterility and functionality of these devices cannot be assured.

Specifications

Table 9 shows the Neurostimulator physical specifications. For detailed descriptions and specifications for other components and accessories, refer to the product literature packaged with those devices.

Table 9. Neurostimulator specifications

Physical Attributes	Height	42 mm
	Length	22 mm
	Thickness	6 mm
	Weight	11 grams
	Volume	5.5 cc
	Radiopaque identifier	AXA
Stimulation Characteristics	Frequency	2-130 Hz
	Pulse Width	60-450 μs
	Amplitude	0-12.5 mA
	Minimum Amplitude Step Size	0.05 mA
	Ramping	0-30 s
	Stimulation Mode	Continuous or Cycling
	Mode of Operation	Current-Controlled
Power Source	Battery	Rechargeable
	Power Source	50 mAh (3.6V)
	Battery life	15 years (open-ended)*

Note: All dimensions are approximate.

*Battery life estimated at nominal and worst case stimulation settings.

Nominal: 1 mA, 14 Hz, 210 µs, continuous stimulation, impedance = 1,600 Ohms.

Worst case: 4 mA, 14 Hz, 210 µs, continuous stimulation, impedance = 1,600 Ohms.

Table 10 shows the materials used in the Neurostimulator kit components that come in contact with human tissue.

Table 10. Human-Contact Materials

Device	Component	Material
Neurostimulator	Neurostimulator case	Titanium-Ceramic
	Neurostimulator header	Epoxy
	Septum and strain relief	Silicone
	Setscrew	Titanium
	Adhesive	Silicone
Torque wrench	Torque wrench handle	Polyetherimide
	Torque wrench shaft	Stainless steel

Note: The Neurostimulator case, which contains the electronics and power source, is hermetically sealed.

X-Ray identification

The radiopaque marker allows physicians to identify the manufacturer and model number under standard x-ray procedures. For the Axonics Neurostimulator, the designated code is AXA, which appears as light characters on a black background (Figure 2).

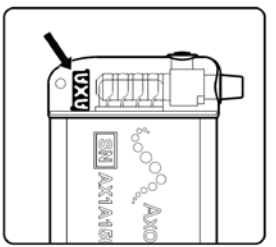

Figure 2: The Axonics Neurostimulator radiopaque marker, “AXA.”

Neurostimulator Implant Procedure

The following section describes the procedure for implanting the Axonics Neurostimulator. This procedure should be performed when an Axonics tined lead has already been implanted.

Procedure supplies

In addition to the general surgical tools required by the physician, the following supplies are needed for the preparation, implantation, programming, and Remote Control pairing of the Neurostimulator:

- Axonics Neurostimulator
- Axonics Charging System

- Axonics Clinician Programmer (CP)
- Axonics Remote Control

⚠ **Caution:** The user should avoid damaging the Neurostimulator and be especially cautious using sharp instruments as damage to the Neurostimulator may require a surgical replacement.

Neurostimulator Preparation

Use the Charger to activate the Neurostimulator. Before opening the sterile Neurostimulator package, the Clinician Programmer (CP) should be used to communicate with the Neurostimulator to verify the ability to communicate and to check battery status. If the Neurostimulator battery is low, the device should be charged through the box before implantation by using the Charger. Refer to the CP and Charging System Manuals for further instructions.

Creating the Neurostimulator pocket

1. The Neurostimulator will be placed in a subcutaneous pocket at the anterior surface of the muscle in the upper buttock area. Create a small incision, slightly larger than the smaller dimension of the Neurostimulator, and then bluntly dissect a subcutaneous pocket.

Notes:

- The Neurostimulator should be placed no deeper than 3.0 cm (about 1 in) below the skin and should be parallel to the skin. If the Neurostimulator is too deep or is not parallel to the skin, charging and/or programming the device may be unsuccessful.
- The Neurostimulator should be implanted

horizontally **(Figure 3)** with the ceramic side farthest from the patient's midline to facilitate charging and programming.

- For a patient with another neurostimulator already implanted, the neurostimulators should be placed as far away as practical and separated by a minimum of 20 cm (8 in).

⚠ **Cautions:**

- The Neurostimulator implant site should be irrigated with antibiotic solution, and it is recommended that IV antibiotics be administered perioperatively. Do not soak the Neurostimulator in antibiotic solution as this may affect lead connections.
- The Neurostimulator has been sterilized. The Neurostimulator should not be placed on any non-sterile surface. The Neurostimulator should not be placed on skin. An infection may require surgical removal of the implanted system.

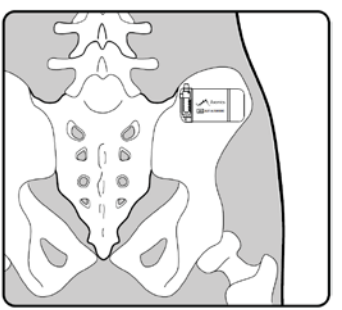

Figure 3: Axonics Neurostimulator implantation position.

2. Use the tunneling tool to create a tunnel from the lead incision site to the neurostimulator pocket. Refer to the Tined Lead Manual for detailed tunneling and lead implant instructions.

Connecting the lead to the Neurostimulator

1. The components should be wiped and dried to remove any fluids before making the connections. If necessary, use sterile water or a non-ionic antibiotic solution, then wipe dry.

⚠ **Caution:** Failure to completely dry the components could lead to undesired stimulation, intermittent stimulation, or loss of therapy.

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2. Ensure that the Neurostimulator connector block is dry and clean.
3. Use the torque wrench to turn the setscrew counterclockwise to back up the setscrew. Do not remove the setscrew from the connector block **(Figure 4)**

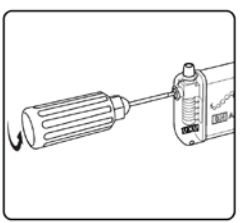

Figure 4: Use the torque wrench to turn the setscrew counterclockwise to **back up** the Neurostimulator setscrew and allow for insertion of the lead.

4. Insert the lead into the Neurostimulator connector block

until fully seated and the lead cannot be inserted further. Marker D on the lead should be inside the Neurostimulator strain relief **(Figure 5)**. The retention sleeve on the tined lead should be positioned under the Neurostimulator setscrew.

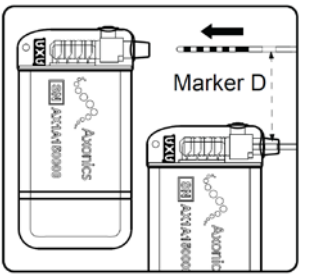

Figure 5: Insert lead fully into the Neurostimulator connector block.

⚠ **Cautions:**

- Avoid pulling the lead body taut when implanted.
- Do not attempt to insert the lead into the Neurostimulator if the setscrew is not sufficiently retracted as doing so may cause damage to the lead and/or cause the lead to not seat fully into the connector block.
- Ensure that the setscrew tightens on the retention sleeve, not an electrode. Tightening the setscrew onto the contact could damage the contact, leading to lack of therapy.

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5. Fully insert the torque wrench into the hole of the Neurostimulator connector block. Tighten the setscrew by turning the torque wrench clockwise until it clicks **(Figure 6)**.

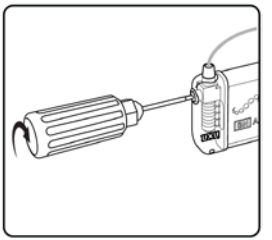

Figure 6: Secure the lead by tightening the setscrew clockwise onto the retention sleeve.

Cautions:

- Ensure that the torque wrench is fully inserted into the setscrew. Otherwise the setscrew may be damaged, which can result in intermittent or loss of stimulation.
- The torque wrench is designed for single use only and cannot be assured to work appropriately if used for multiple surgeries. Discard the torque wrench after use.

Implanting the Neurostimulator

1. Place the Neurostimulator into the subcutaneous pocket. Ensure that the ceramic side is placed away from the patient's midline to ensure good communication with the Remote Control and ease of recharging **(Figure 3)**. The etched writing can face either towards or away from the muscle tissue. Ensure that the lead curves gently away from the Neurostimulator with no sharp bends.

Note: The Neurostimulator should be placed no deeper than 3.0 cm (about 1 in) below the skin and should be parallel to the skin. If the Neurostimulator is too deep or is not parallel to the skin, telemetry and/or charging may be unsuccessful.

Caution: Do not coil excess length in front of Neurostimulator. Wrap excess length around the perimeter of the Neurostimulator **(Figure 7)** or place under the Neurostimulator to minimize interference with telemetry during programming.

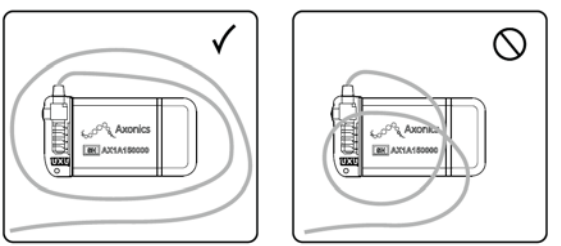

Figure 7: Wrap excess lead around or under, but not on top of, the Neurostimulator.

2. Use the Clinician Programmer to check the impedances and ensure good function and connectivity of the system.

   Notes:

   - The Neurostimulator should be in the subcutaneous pocket during system interrogation to ensure proper readings.
   - Refer to the Clinician Programming Manual for detailed instruction on checking the system integrity and impedances.

3. Use the suture hole in the header to secure the Neurostimulator to the muscle fascia with non-absorbable silk

Completing the implant procedure

1. Close and dress all incisions.
2. Program the patient's Neurostimulator and Remote Control. Refer to the Clinician Programming Manual for more detailed instruction.
3. Give a Remote Control and patient ID card to the patient.

Caution: The patient must carry the Remote Control at all times to be able to adjust or turn off the Neurostimulator.

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4. Complete the system registration paperwork and return to Axonics.
5. Schedule the patient's follow-up visits at regular intervals to ensure that the stimulation is programmed optimally.

Post-surgery treatment

Administer prophylactic antibiotics for 24 hours.

Replacing the Neurostimulator

1. Carefully open the implant site and remove the Neurostimulator from the subcutaneous pocket. Avoid cutting the tined lead to preserve for connection with the new Neurostimulator.
2. Clean the Neurostimulator connector block and lead with sterile water. Wipe both dry with sterile gauze.
3. Use the torque wrench to loosen the setscrew in the Neurostimulator connector block by turning it counterclockwise **(Figure 5)**.
4. Gently remove the lead from the Neurostimulator.

 **Caution:** Replace any device that shows signs of damage, pitting, or corrosion.

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5. Set aside the explanted components, which should be returned to Axonics.
6. Connect the lead and replacement Neurostimulator according to the steps above.

Return explanted devices to Axonics using materials provided.

WIRELESS COMMUNICATION

Model: 1101
IC: 20225-X
FCC ID: 2AEEGX

FCC Compliance

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.

IC Compliance

This device complies with Industry Canada license-exempt RSS standard(s). Operation is subject to the following two

conditions: (1) this device may not cause interference, and (2) this device must accept any interference, including interference that may cause undesired operation of this device.

FCC and IC Compliance

This device may not interfere with stations operating in the 400.150–406.000 MHz band in the Meteorological Aids, Meteorological Satellite, and Earth
Exploration Satellite Services and must accept any interference received, including interference that may cause undesired operation.

Note: Changes and modifications to the Neurostimulator 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 402-405 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 implant for successful communication.

Wireless Security: The Neurostimulator 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.

CUSTOMER SERVICE

For questions regarding the Axonics SNM System, call our Customer Support Center toll-free at +1-877-929-6642.

Additional information and product manuals can be found at our website: www.axonics.com

EC REP

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