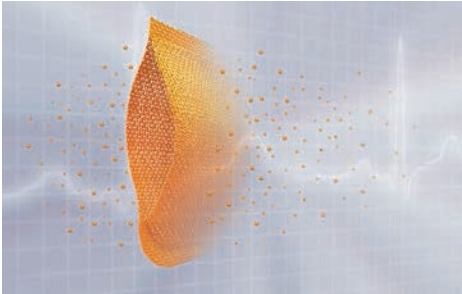


PERFECT-POCKET™ PROTECTION

WITH THE NEW, REVOLUTIONARY AIGISRx® R

FULLY RESORBABLE ANTIBACTERIAL ENVELOPE

Besirezorbuojanti įmautė
elektrokardiostimuliatoriaus implantacijai,
impregnuota antibiotikais

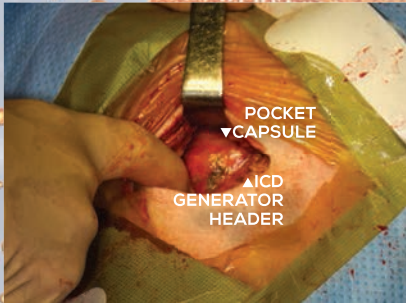


Stabilizes CIED Placement Helps Prevent CIED Infection

Unique Bioresorbable Mesh

- Fully resorbs into the body in ~9 weeks¹
- Requires no adjustment to standard surgical techniques during replacement or revision procedure

organizme rezorbuojasi per 9 savaites

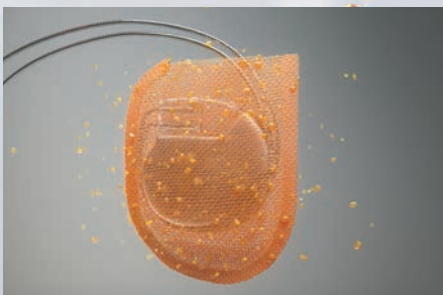


Bioresorbability of AIGISRx R in Patients

- Dual chamber ICD implanted with AIGISRx R Antibacterial Envelope
- Dislodged lead revised ~5 weeks later
- No visible remnant of the AIGISRx R, generator easily removed

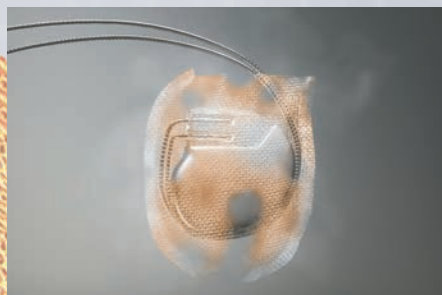
Photos courtesy of Francois Philippon, MD Laval University Hospital, Quebec City, Canada

Time sequence demonstrating bioresorbability of AIGISRx R after ~9 weeks



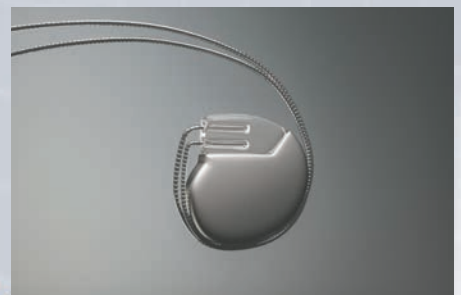
AIGISRx R after implantation²

Envelope is eluting minocycline & rifampin.



AIGISRx R at 4 weeks³

Envelope is dissolving into fragments.



AIGISRx R at ~9 weeks¹

Mesh has no physical presence and is fully resorbed.

NOW, FULLY RESORBABLE.

PLUS ALL THE PROTECTION OF THE ORIGINAL AIGISRx

Designed to Aid in the Stabilization of CIED Placement

- Use of the AIGISRx R Antibacterial Envelope anchors the CIED in the tissue pocket.¹
- Reduces chance of device migration or erosion due to Twiddler's Syndrome.^{1,4}
- AIGISRx R and AIGISRx are safe and effective at stabilizing a CIED generator within a tissue pocket and preventing migration. There is no clinically significant difference between their performances.¹

Helps Prevent CIED Infections

- AIGISRx R contains the antimicrobial agents minocycline and rifampin which are released locally into the tissue to help reduce CIED infection following implantation.
- The amount of drug dose contained in the AIGISRx R is <10% of the recommended daily oral dose of minocycline and rifampin.⁵
- The AIGISRx R and the original AIGISRx have identical antibiotic efficacy.

PATHOGENS RESPONSIBLE FOR CIED INFECTIONS	SINGLE-AGENT THERAPY		AIGISRx R AND AIGISRx ⁵⁻⁸
	cefazolin	vancomycin	minocycline and rifampin
Coagulase (-) Staphylococcus (eg, <i>S. epidermidis</i>)			
Methicillin-sensitive <i>S. aureus</i> (MSSA)			
Methicillin-resistant <i>S. aureus</i> (MRSA)			
<i>Escherichia coli</i>			
<i>Haemophilus influenzae</i>			
<i>M. catarrhalis</i>			
<i>Corynebacterium jeikeium</i>			

- Multiple studies show that patients at high-risk for CIED infection who are implanted with the AIGISRx Antibacterial Envelope had 70% to 100% fewer device infections than similar patients who did not receive the AIGISRx.^{9-11,17}

AIGISRx R

AIGISRx R Perfect-Pocket™ Protection

- Fully Resorbs in ~9 Weeks.¹
- Specifically designed to aid in the stabilization of CIED Placement.
- Combination of rifampin & minocycline has been shown to reduce medical device infections.¹²⁻¹⁶
- Associated with 70% to 100% fewer infections compared to patients without it.⁹⁻¹¹
- Cost Effective—Your facility may reduce costs by as much as \$100,000 for every 100 Envelopes used with your high-risk CIED patients.^{3,10,17-19}



AIGISRx R Medium Fully Resorbable Antibacterial Envelope
Size: 2.5" (6.3cm) x 2.7" (6.9cm)
SKU # CMRM-6122US-B



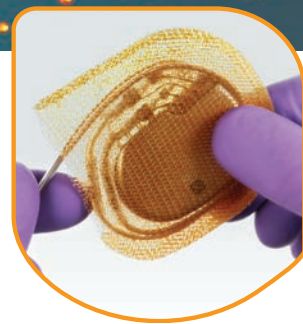
AIGISRx R Large Fully Resorbable Antibacterial Envelope
Size: 2.9" (7.4cm) x 3.3" (8.5cm)
SKU # CMRM-6133US-B

¹ Huntington Study TR-2011-054. ² Huntington Study TR-2013-001. ³ Data on file, 093013-1. ⁴ Hirsh J. *EP Lab Digest*. July 2012; 12(7); Clinical Case Report; Recurrent Twiddler's Syndrome. ⁵ Gilbert DN et al. *The Sanford Guide to Antimicrobial Therapy*. 42nd ed. 2012: Antimicrobial Therapy Inc.; Hyde Park, VT. ⁶ Zinner SH et al. *J Infect Dis*. 1981; 144(4):365-371. ⁷ Darouiche RO et al. *Int J Antimicrob Agents*. 1995; 6(1):31-36. ⁸ Segreti J et al. *Diagn Microbiol Infect Dis*. 1989; 12(3):253-255. ⁹ Bloom H et al. *Pacing Clin Electrophysiol*. 2011; 34(2):133-142. ¹⁰ Kolek MJ et al. *Pacing Clin Electrophysiol*. 2013; 36(3):354-361. ¹¹ Henrickson CA, Citadel & Centurion Studies. Presented at the Late Breaking Clinical Trials session at the European Heart Rhythm Association (EHRA), *Europace*. 2013. ¹² Hanna H et al. *J Clin Oncol*. 2004; 22(15):3163-3171. ¹³ Leon C et al. *Intensive Care Med*. 2004; 30(10):1891-1899. ¹⁴ Zabramski JM et al. *J Neurosurg*. 2003; 98(4):725-730. ¹⁵ Chatzinikolaou I et al. *Am J Med*. 2003; 115(5):352-357. ¹⁶ Road I et al. *Ann Intern Med*. 1997; 128(4):267-274. ¹⁷ Mittal S et al. 2013 HRS Scientific Session, PO 05-43, NY/NJ Valley Health System. ¹⁸ Inpatient Prospective Payment System (IPPS) Final Rule FY13. ¹⁹ Data on file, 092713-1.

MKT-23-211 Rev 1B

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TYRX, Inc., 1Deer Park Drive, Suite G, Monmouth Junction, NJ 08852 Customer Service: 866.908.8979 | TYRX.com | HeartDeviceInfection.com



Product:

AIGISRx® is an Antibacterial Envelope is made from knitted polypropylene mesh substrate, coated with a polyarylate bioresorbable polymer containing two antimicrobial agents, minocycline and rifampin. AIGISRx is a dual component (resorbable and non-resorbable), sterile prosthesis designed to reduce infection and to stabilize the implantable pacemaker or defibrillator when implanted in the body.

AIGISRx Polypropylene Mesh:

Performance Properties

Burst Strength = 49.3 PSI - 180 PSI

Break Strength ≥ 150N

Product Indications:

AIGISRx is intended to securely hold the pacemaker pulse generator or defibrillator in order to create a stable environment when implanted in the body. AIGISRx contains the antimicrobial agents, rifampin and minocycline, which have been shown to reduce infection in an *in vivo* model of bacterial challenge following surgical implantation of the generator or defibrillator. This device is only intended to be used in conjunction with pacemakers and implantable defibrillators.

Non-resorbable Mesh Substrate:

A large-pore mesh knitted from monofilament polypropylene filaments, similar in composition and diameter to 5-0 suture. The knitted mesh comprises over 90% of the entire AIGISRx device by weight.

Resorbable Polymer Coating:

A bioresorbable, biocompatible polymer based upon the amino acid, tyrosine, which breaks down linearly, primarily via hydrolysis and is resorbed in approximately 140 days. This bioresorbable polymer breaks down into naturally occurring components which are considered Generally Regarded As Safe (GRAS). The primary purpose of this polymer is to act as a carrier for the antimicrobial agents, minocycline and rifampin. The tyrosine polymer and drug combination, which are spray coated onto the polypropylene mesh, comprise the remaining 10% of the entire AIGISRx device by weight.

Antibiotics:

Minocycline is a bacteriostatic antimicrobial which inhibits protein synthesis of the cell wall.

Minocycline has been shown to be effective against Gram positive (+) bacteria such as *S. aureus* and *S. pneumoniae* and Gram negative (–) bacteria such as *E. coli*, *E. aerogenes*, *H. influenza* and *A. baumannii*.

Minocycline dose per AIGISRx device: up to 11mg (Pacemaker), 16mg (ICD). Sustained released over 7 to 10 days.

Rifampin is a bacteriocidal antimicrobial which interferes with DNA-dependent RNA polymerase activity.

Rifampin has been shown to be effective against Gram positive (+) bacteria such as *S. aureus* (including MRSA) and *S. epidermidis* and Gram negative (–) bacteria such as *H. influenza*.

Rifampin dose per AIGISRx device: up to 11mg (Pacemaker) 16mg (ICD). Sustained released over 7 to 10 days.

AIGISRx PM Antibacterial Pacemaker Envelope

Size: 2.5" (6.4cm) x 2.75" (7.0cm)

SKU # CMRM-3122-B (box of 6 individuals)

Single Use Only: Do Not Resterilize

Storage: Store between 36–77° F (2–25° C)

Each AIGISRx polymer-coated envelope is placed in a Tyvek folder insert which is packaged inside a single-barrier foil pouch.

AIGISRx ICD Antibacterial Defibrillator Envelope

Size: 3.0" (7.6cm) x 3.35" (8.5cm)

SKU # CMRM-3133-B (box of 6 individuals)

Single Use Only: Do Not Resterilize

Storage: Store between 36–77° F (2–25° C)

Each AIGISRx polymer-coated envelope is placed in a Tyvek folder insert which is packaged inside a single-barrier foil pouch.

For full prescribing information see minocycline and rifampin package inserts. For full prescribing information for AIGISRx, including warnings, cautions and contraindications, see package insert.

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a licensed medical practitioner.

The TYRX polymers are protected under one or more of these patents: U.S. Patent Nos. 6120491, RE37160

MKT-23-097 Rev 4



Medtronic

TYRX™

Antibacterial Envelope

TYRX™ Antibacterial Envelope

(Tyrosine Polyarylate-coated, Monofilament Polypropylene Mesh Envelope
Containing the Antimicrobials Rifampin and Minocycline)

INSTRUCTIONS FOR USE USA

STERILE: Contents sterile unless package has been opened or damaged. Single Use Only. Do Not Resterilize.

CAUTION: Read instructions prior to use.

Rx Only

PRODUCT DESCRIPTION

The TYRX™ Antibacterial Envelope is a dual component (absorbable and non-absorbable), sterile prosthesis designed to hold a pacemaker pulse generator or defibrillator to create a stable environment when implanted in the body.

The antibacterial envelope is constructed of knitted filaments of polypropylene that are coated with an absorbable polyarylate polymer.

The antibacterial envelope absorbable polymer coating contains the antimicrobial agents rifampin and minocycline in concentrations of 86 µg/cm².

INDICATIONS FOR USE

The antibacterial envelope is intended to securely hold a pacemaker pulse generator or defibrillator in order to provide a stable environment when implanted in the body. The antibacterial envelope contains the antimicrobial agents rifampin and minocycline which have been shown to reduce infection in an *in vivo* model of bacterial challenge following surgical implantation of the generator or defibrillator. This device is only intended to be used in conjunction with pacemakers and implantable defibrillators.

ACTIONS

The antibacterial envelope is constructed of knitted filaments of polypropylene that are coated with a absorbable polyarylate polymer. The purpose of the absorbable coating is to act as a carrier for the antimicrobial agents. Once placed, the polymer absorbs in approximately 140 days, leaving a lightweight permanent mesh incorporated into the tissue.

The antibacterial envelope releases the antimicrobial agents rifampin and minocycline for a minimum of 7 days to reduce the risk of infection of the implanted pulse generator following surgery. In *in vitro* studies, the antibacterial envelope demonstrated antimicrobial activity against methicillin-resistant *Staphylococcus aureus* (MRSA), *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Acinetobacter baumannii*, *Enterobacter aerogenes*, and *Proteus mirabilis*.

The antibacterial envelope also demonstrated *in vivo* effectiveness in reducing infections in a series of studies in which a pulse generator canister placed into an antibacterial envelope and generator canister alone (Control) were implanted into appropriate models of infectivity (dogs or rabbits). Both the antibacterial envelope and the Control groups were inoculated with bacteria and observed for a minimum of 7 days to validate the presence of infection in the animals. The bacteria tested included *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Acinetobacter baumannii*, and *Escherichia coli* which represent a majority of the infections reported in pacemaker-related endocarditis.

It should be noted that the *in vitro* and *in vivo* activity of the antibacterial envelope antimicrobials is variable against non-*epidermidis* strains of coagulase-negative staphylococci.

CONTRAINDICATIONS

The antibacterial envelope is **NOT** indicated for use in the following situations:

- Allergy or history of allergy to tetracyclines, or rifampin, or polypropylene.
- In patients with systemic lupus erythematosus (SLE) because minocycline has been reported to aggravate this condition.
- Use of the antibacterial envelope in contaminated or infected wounds.

WARNINGS

This device is supplied sterile. Inspect the packaging to be sure that it is intact and undamaged prior to use.

This device is for single use only. Do not resterilize. Product should be used once the exterior foil wrapper has been broken. Do not store for later use. Unused portions of the prosthesis should be discarded.

If the unused prosthesis has been in contact with instruments or supplies used on a patient or contaminated with bodily fluids, discard with care to prevent risk of transmission of any disease.

The use of any permanent mesh in a contaminated or infected wound could lead to fistula formation and extrusion of the prosthesis. If infection develops, treat the infection aggressively as per standard practice. The prosthesis may not have to be removed. An unresolved infection may require removal of the prosthesis.

As in any antimicrobial therapy, the possible teratogenic potential in women capable of having children should be carefully weighed against the benefit of therapy.

This device has not been evaluated in pediatric patients.

The use of this product in patients with compromised hepatic and renal function, or in the presence of hepatotoxic or renal toxic medications, should be carefully considered since rifampin and minocycline can cause additional stress on the hepatic and renal systems. Patients who are implanted with this device and are also taking methoxyflurane should also be carefully monitored for signs of renal toxicity.

Patients who are implanted with this device who are also taking warfarin should have their International Normalized Ratio (INR) time monitored because tetracyclines have also been reported to potentiate the anticoagulant effect of warfarin. The use of this product in patients being treated with thionamides, isoniazid, or halothane should be carefully considered due to potential hepatic side effects that have been reported in patients using these drugs and higher doses of rifampin.

The contraindications, warnings and precautions applicable to the use of specific antibiotic prophylaxis should be followed when prophylaxis is administered in conjunction with implantation of a pacemaker pulse generator or defibrillator enclosed in an antibacterial envelope.

Development of a hypersensitivity reaction should be followed by removal of the device and appropriate treatment initiated at the discretion of the attending physician.

Use of the antibacterial envelope in contaminated wounds is not recommended. The device is not indicated for the treatment of infection. Because the antibacterial envelope is impregnated with a combination of the antimicrobial agents rifampin (a derivative of rifamycinB) and minocycline (a derivative of tetracycline), the contraindications, warnings, and precautions regarding the use of these antimicrobials apply and should be adhered to when using this device.

CAUTIONS

Only physicians qualified in the placement of pulse generators or defibrillators should use this prosthesis.

Rx Only

There are no known interactions between rifampin and minocycline. As with many drugs, the effectiveness of minocycline and rifampin may be reduced after direct contact with solutions containing iodine.

Do not alter usual practice of pre-, peri-, or post-operative administration of local or systemic antibiotics.

COMPLICATIONS AND ADVERSE REACTIONS

Possible complications for these procedures include bleeding and infection. (See **WARNINGS**.) There is currently no long-term data available to determine whether tissue reactions to the antibacterial envelope will be equivalent to the Parsonnet™ Pacemaker Pouch. As with any surgical procedure involving the implantation of a pacemaker/defibrillator, there may be complications including seroma, adhesions, hematoma, inflammation, extrusion, or fistula formation. If infection develops, treat the infection aggressively as per standard practice, including removal of the prosthesis, if indicated. Please report any device-related adverse events to Medtronic, Inc. at 1-800-848-9300.

STORAGE: The antibacterial envelope should be stored between 36 – 77 °F (2 – 25 °C). Do not freeze.

HANDLING: Use clean, sterile gloves and/or atraumatic instruments when handling the mesh.

MAINTAINING ASEPSIS

To help maintain strict asepsis during surgery, special precautions and careful preoperative site preparations are necessary. Any postoperative infection should be aggressively treated as soon as possible. Any unresolved infection may require removal of the prosthesis.

PREPARATION

It is recommended that the antibacterial envelope be completely immersed for a few seconds in standard irrigation solution to facilitate placement.

INSERTION TECHNIQUE

Prepare the pulse generator or defibrillator as per manufacturer's instructions, making sure to secure the leads. Slide the pulse generator/defibrillator into the opening in the envelope with lead wires emerging straight out as shown in Figure 1. It is important to make sure that the pocket is created large enough to accommodate the additional volume of the antibacterial envelope, to ensure that closure of the incision does not place too much tension on the sutures on the adjacent skin, and that the layers of suture do not inadvertently ensnare the envelope. Place generator/defibrillator into the patient as per standard practice. If the dimensions of the pulse generator/defibrillator are larger than the opening, but of similar dimension to the antibacterial envelope, the opening can be widened to accommodate placement. (NOTE: The antibacterial envelope cannot be used with generators and defibrillators that are larger than its internal dimensions.) For generators and defibrillators that are significantly smaller than the antibacterial envelope, the generator/defibrillator should be placed as shown in Figure 2. Nonabsorbable or absorbable monofilament sutures can be used to tack the opening of the envelope to secure the generator/defibrillator prior to implantation.

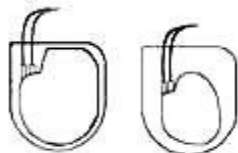


Figure 1 Figure 2

REMOVAL OF PULSE GENERATOR FROM INCORPORATED ENVELOPE

It may be necessary to remove the pacemaker or defibrillator from the envelope after a period of implantation. First, surgically expose the envelope. Make an incision on the flat side of the envelope, approximately the width of the pacemaker or defibrillator. Disconnect the electrode leads. Remove the pacemaker/defibrillator through the opening in the side of the envelope. If required, insert a drainage tube. A new pacemaker/defibrillator may be inserted into the envelope through the side opening. Connect the electrical leads. Suture the envelope closed. Complete the procedure following standard accepted surgical techniques. Familiarization with the device and following proper surgical techniques are important when explanting a device. Always use standard of care subject to the patient's condition and the surgical presentation in removing an implant.

TRACEABILITY

A traceability label, which identifies the type, size and lot number of the prosthesis, is attached to the foil label in every package. This traceability label should be peeled off and affixed to the patient's permanent medical record to clearly identify the device that was implanted.

HOW SUPPLIED

The antibacterial envelope is supplied sterile in foil pouches in two sizes, a Medium and Large envelope.



Manufactured by

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Monmouth Junction, New Jersey 08852, USA

Manufactured for
Medtronic, Inc.
710 Medtronic Parkway
Minneapolis, MN 55432
www.medtronic.com
763-514-4000

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LBL-0855 Rev 4