BC "MOLDINDCONBANK" S.A.
Filiala "Invest"

Republica Moldova, MD-2068
mun. Chişinău, bd. Moscovei, 14/1
Tel. : (373-22) 43-44-81, 43-46-24
Fax : (373-22) 43-44-22
cod: MOLDMD2X329

Data 14. IAN. 2016
Nr. 03/2 – 19/23

Республика Молдова, MD-2068
мун. Кишинэу, бул. Московей, 14/1
Тел. : (373-22) 43-44-81, 43-46-24
Факс : (373-22) 43-44-22
код: MOLDMD2X329

Filiala „Invest" BC „Moldindconbank" SA confirmă existența contului curent in moneda nationala al **"BIOSISTEM MLD" S.R.L. (c/f 1010600028048)**, cu **IBAN MD95ML0000000022514292 43**.

Codul băncii MOLDMD2X329.

Director **Nina Țurcan**

Director financiar **Nina Balmuş**

Ex. Diana Brinza
Tel. 43-45-96

Digitally signed by Poiata Vitalie
Date: 2024.03.29 14:02:26 EET
Reason: MoldSign Signature
Location: Moldova

REPUBLICA MOLDOVA

CERTIFICAT DE ÎNREGISTRARE

Societatea cu Răspundere Limitată "BIOSISTEM MLD"
ESTE ÎNREGISTRATĂ LA CAMERA ÎNREGISTRĂRII DE STAT

Numărul de identificare de stat - codul fiscal
1010600028048

Data înregistrării **12.08.2010**

Data eliberării **12.08.2010**

Svirepova Ludmila, registrator

Funcția, numele, prenumele persoanei care a eliberat certificatul

semnătura

MINISTERUL JUSTIȚIEI AL REPUBLICII MOLDOVA
CAMERA ÎNREGISTRĂRII DE STAT I.S.
1004600077777
104

MD 0101250

AGENŢIA SERVICII PUBLICE

Departamentul înregistrare şi licenţiere a unităţilor de drept

EXTRAS

din Registrul de stat al persoanelor juridice

Nr. **531522** data **15.09.2023**

Denumirea completă: **Societatea cu Răspundere Limitată "BIOSISTEM MLD"**
Denumirea prescurtată: **"BIOSISTEM MLD" S.R.L.**
Forma juridică de organizare: **Societate cu răspundere limitată,**
Numărul de identificare de stat şi codul fiscal (IDNO): **1010600028048**
Data înregistrării de stat: **12.08.2010**
Sediul: **MD-2001, str. Albişoara, 16/1, ap. 7, mun. Chişinău, Republica Moldova.**
Obiectul principal de activitate:
1. Activitatea farmaceutică; importul şi (sau) producerea articolelor de parfumerie şi cosmetică
2. Fabricarea, comercializarea, asistenţa tehnică, repararea şi verificarea articolelor de tehnică şi optică medicală
3. Acordarea asistenţei medicale de către instituţiile medico-sanitare private
4. Comerţul cu ridicata al calculatoarelor,echipamentelor periferice şi software-ului
5. Întreţinerea şi repararea maşinilor de birou şi a tehnicii de calcul
6. Consultaţii în domeniul sistemelor de calcul

Capitalul social: **5400** lei.

Administrator: **POIATA VITALIE, IDNP 0983103892591,**

Asociaţii:
1. POIATA VITALIE, IDNP 0983103892591, cota 1803,60 lei, ce constituie 33,4%
Beneficiar efectiv:
1.1. POIATA VITALIE, IDNP 0983103892591,

2. NASEDCHIN ALEXANDR, IDNP 2002001070747, cota 1798,20 lei, ce constituie 33,3%
Beneficiar efectiv:
2.1. NASEDCHIN ALEXANDR, IDNP 2002001070747,

3. KOJEVNIKOV DMITRII, IDNP 0972305012362, cota 1798,20 lei, ce constituie 33,3%
Beneficiar efectiv:
3.1. KOJEVNIKOV DMITRII, IDNP 0972305012362

Prezentul extras este eliberat în temeiul art.34 al Legii nr.220-XVI din 19 octombrie 2007 privind înregistrarea de stat a persoanelor juridice şi a întreprinzătorilor individuali şi confirmă datele din Registrul de stat la data de: **15.09.2023**.

Registrator în domeniul înregistrării de stat

Digitally signed by Rusu Diana
Date: 2023.09.15 16:44:17 EEST
Reason: MoldSign Signature
Location: Moldova

Rusu Diana

EB 0461494

Date cu caracter personal

BIOSISTEM-MLD S.R.L.
c/f 1010600028048; adresa: or. Chișinău, str. Albișoara 16/1 of.7
tel.+373-22-808-517, +373-22-808719, fax: +373-22-808-519.
Web: www.biosistem-mld.com; e-mail: biosistem.mld@gmail.com

Lista fondatorilor Biosistem-mld SRL

Nr.	Nume, Prenume	IDNP
1.	Vitalie Poiata	0983103892591
2.	Alexandr Nasedchin	2002001070747
3.	Dmitrii Kojevnikov	0972305012362

(en) ENGLISH

Instructions for Use

ARTIVION™ | BioGlue®

www.artivion.com/eifu/bioglue

A printed version of the Instructions for Use will be provided within seven days upon request to BioGlue customer service through any of the contact means listed below.

Phone: 888.427.9654 • Fax: 770.590.3753
Email: customer_service.us@artivion.com

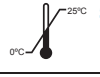
ARTIVION™
1655 Roberts Boulevard, NW
Kennesaw, Georgia 30144, USA
Phone: +1 (888) 427-9654
FAX +1 (770) 590-3753
www.artivion.com

EC REP
JOTEC GmbH
Lotzenäcker 23
D-72379 Hechingen, Germany

CE 0124

L09330.000 (2022-10-28)

EXPLANATION OF SYMBOLS

	Manufacturer		Consult instructions for use / Consult electronic instructions for use
	Date of manufacture		Caution
	EU Authorized Representative		Caution: Federal (USA) Law restricts this device to sale by or on the order of a physician
	Importer		Non-pyrogenic
	Medical Device		Contains biological material of animal origin
	Do not use if package is damaged		MR safe
	Single sterile barrier system		Catalogue number
	Double sterile barrier system		Batch code
	Sterilized using ethylene oxide		Unique device identification
	Sterilized using irradiation		Use-by date
	Do not re-sterilize		Country of manufacture
	Do not re-use		Quantity
	Temperature limit		

PRODUCT DESCRIPTION

BioGlue® Surgical Adhesive is a two-component surgical adhesive composed of solutions of purified bovine serum albumin and glutaraldehyde. Once dispensed, the adhesive solution (in predefined ratio) are mixed within the applicator tip where cross-linking begins. The glutaraldehyde molecules covalently bond (cross-link) the BSA molecules to each other and, upon application, to the tissue proteins at the repair site, creating a flexible mechanical seal independent of the body's clotting mechanism. BioGlue Surgical Adhesive (hereinafter BioGlue) begins to polymerize within 20 to 30 seconds and reaches its bonding strength within 2 minutes. BioGlue also adheres to synthetic graft materials via mechanical interlocks within the interstices of the graft matrix.

The following accessories are sold separately to aid in the delivery of BioGlue Surgical Adhesive:

Product Code	Product Description
BGAT-SY	Applicator tip
BGAT-10-SY	Syringe extender tip - 10cm
BGAT-27-SY	Syringe extender tip - 27cm
BGST-12	Spreader applicator tip - 12mm
BGST-16	Spreader applicator tip - 16mm
BGDTE-10	Delivery tip extension - 10cm
BGDTE-27	Delivery tip extension - 27cm
BGDTE-35	Delivery tip extension - 35cm

BioGlue syringes are available in 3 configurations - 2mL, 5mL, and 10mL. Each syringe is composed of bovine serum albumin (BSA) and glutaraldehyde solutions in a 4:1 ratio, respectively. The BSA solution is amber in color and free-flowing. The glutaraldehyde solution is clear and also free-flowing.

The specification for the BSA solution is a 45% (weight/volume ratio) solution. The maximum 45% BSA solution target weights for each size are: 2.71 grams (2mL syringe), 4.75 grams (5mL syringe), and 9.50 grams (10mL syringe). Based on these targets, the maximum quantity of animal origin material coming into contact with the patient when using a single device is 1.22 grams (2mL syringe), 2.14 grams (5mL syringe), and 4.23 grams (10mL syringe) for each configuration.

The specification for the glutaraldehyde solution is a 10% (weight/volume ratio) solution. The maximum 10% glutaraldehyde solution target weights for each size are: 0.63 grams (2mL syringe), 1.10 grams (5mL syringe), and 2.16 grams (10mL syringe). Based on these targets, the maximum quantity of glutaraldehyde coming into contact with the patient when using a single device is 0.06 grams (2mL syringe), 0.11 grams (5mL syringe), and 0.22 grams (10mL syringe) for each configuration.

INDICATIONS / INTENDED PURPOSE

BioGlue Surgical Adhesive is indicated for use as an adjunct to standard methods of surgical repair (such as sutures, staples, and/or patches) to adhere, seal, and/or reinforce soft tissue. Indicated soft tissues are cardiac, vascular, pulmonary, and dural.

TARGET PATIENT POPULATION

Adult patients undergoing surgery who require an adjunct to standard method of surgical repair to bond, seal, and/or reinforce cardiac, vascular, dural, and pulmonary tissue.

INTENDED USERS

BioGlue Surgical Adhesive is intended to be used by healthcare professionals, such as surgeons, qualified in the appropriate indication.

PERFORMANCE CHARACTERISTICS

- BioGlue reaches full bonding strength within 2 minutes.[1]
- BioGlue Surgical Adhesive forms strong covalent bonds with tissue and mechanically interlocks with synthetic graft material. These strong bonds lead to BioGlue having a recorded burst strength of at least 560mmHG in in vitro studies. [1,3,4,5]

In large vascular and cardiac procedures where BioGlue was used:

- Decrease in anastomotic bleeding when compared to standard repair technique.[12]

In pulmonary, large vascular and cardiac procedures where BioGlue was used:

- Reduction in ICU and hospital stays when compared to standard surgical technique.[12,19, 23]

In aortic dissection repair where BioGlue was used:

- Fewer pledgets, hemostatic agents, and make-up stitches were required when compared standard surgical technique. [17]
- Operating room time, cross clamp time, circulatory arrest time, bypass time were reduced when compared to surgical technique.[18.19]
- The use of platelets, plasma, and blood cells were reduced when compared to standard surgical technique.[17,19]

In pulmonary procedures where BioGlue has been used:

- BioGlue has been shown to be effective in sealing air leaks when applied to a deflated or inflated lung. [6,7,8,9]
- Air leak duration was reduced when compared to standard surgical repair.[6,8,23]

In dural procedures where BioGlue has been used:

- CSF leaks were reduced when compared to standard surgical repair.[20,21,22]

BioGlue Surgical Adhesive Accessories aid in the delivery of BioGlue.

CLINICAL BENEFITS

In large vascular, cardiac, pulmonary, and dural procedures where BioGlue was used:

- Pseudoaneurysm rates have been shown to be lower when compared to published literature on standard repair technique.[11,14,15]
- Complication rates have been shown to be lower when compared to published literature on standard repair technique.[12, 2,23, 18]
- Mortality rates have been shown to be lower when compared to reported literature on standard repair technique. [10,11,12,13,16]

CONTRAINDICATIONS

BioGlue is contraindicated for use in cerebrovascular repairs and any intra-luminal areas. BioGlue is not for patients with known sensitivity to materials of bovine origin.

WARNINGS ⚠

- Do not use BioGlue as a substitute for sutures or staples in tissue approximations.
- Do not use BioGlue in a manner that would contact or obstruct circulating blood flow during or after application. BioGlue entering the circulation can result in local or embolic vascular obstruction.
- Do not use BioGlue in a manner that would obstruct circulating air or other luminal fluid flow during or after application.
- Avoid contact with nerves, eyes, or other tissue not intended for application.
- An animal study[24] has shown that direct application of BioGlue to the exposed phrenic nerve can cause acute nerve injury. A separate animal study[25] has shown that direct application of BioGlue to the surface of the sinoatrial node (SAN) of the heart can cause coagulation necrosis that extends into the myocardium, which could reach underlying conduction tissue and may cause acute, focal SAN degeneration. Subsequent animal studies[26,27] have demonstrated that chlorhexidine gluconate gel can protect the phrenic nerve, the myocardium, and the underlying SAN from potential injury from BioGlue use.
- Do not use BioGlue if staff is not adequately protected (e.g., wearing gloves, mask, protective clothing, and safety glasses). Unreacted glutaraldehyde may cause irritation to eye, nose, throat, or skin; induce respiratory distress; and cause local tissue necrosis. Prolonged exposure to unreacted glutaraldehyde may cause central nervous system or cardiac pathology. If contact occurs, flush affected areas immediately with water and seek medical attention.
- Polymerized BioGlue has space occupying properties. When used improperly, or applied incorrectly, serious adverse events have been reported relating to compression of adjacent anatomic structures. BioGlue should be used only when complete visualization of the target application location is possible, when it is properly primed to achieve optimal viscosity, and a minimal amount is used. Please see the *Indications/Intended Purpose* and *Directions for Use* sections on this label.
- Minimize use of BioGlue in patients with abnormal calcium metabolism (e.g. chronic renal failure, hyperparathyroidism). Glutaraldehyde-treated tissue has an enhanced propensity for mineralization. Laboratory experiments indicate that unreacted glutaraldehyde may have mutagenic effects.
- Do not use BioGlue in the presence of infection and use with caution in contaminated areas of the body.
- Exercise caution with repeat exposure of BioGlue in the same patient. Hypersensitivity reactions are possible upon exposure to BioGlue. Sensitization has been observed in animals.
- BioGlue contains a material of animal origin, which may be capable of transmitting infectious agents.
- The use of BioGlue in pregnant/breast feeding women has not been studied.
- BioGlue syringe and BioGlue accessories are single-use devices and should not be used in more than one patient.
- The use of BioGlue in pediatric patients has not been studied. BioGlue should not be applied circumferentially to tissue and may not allow that tissue to grow or expand.
- The suitability of BioGlue for treatment of Bronchopleural Fistula (BPF) or Lymphatic Leakage is not confirmed by sufficient data.
- When BioGlue is used in conjunction with any other material, the instructions for both products should be carefully reviewed and adhered to.

PRECAUTIONS ⚠

- It is recommended that surgical gloves, sterile gauze pads/towels, and surgical instruments be maintained moist to minimize the potential for BioGlue inadvertently adhering to these surfaces.
- BioGlue syringe, applicator tips, spreader tips, and syringe extender tips are for single patient use only. Do not re-sterilize.
- Do not use if packages have been opened or damaged.

- Take care not to spill contents of the syringe.
- Do not compress the syringe plunger while attaching it to the syringe.
- Do not apply BioGlue in a surgical field that is too wet. This may result in poor adherence.
- Avoid tissue contact with material expelled from applicator during priming.
- BioGlue polymerizes rapidly. Priming must occur quickly, followed immediately by the application of BioGlue. Pausing between priming and application can cause polymerization within the applicator tip.
- Do not use blood saving devices when suctioning excess BioGlue from the surgical field.
- Clamp and depressurize vessels prior to applying BioGlue to targeted anastomoses.
- To prevent the entrance of BioGlue into the cardiovascular system, avoid any negative pressure during application and polymerization of BioGlue. For example, left ventricular vents should be turned off prior to the application of BioGlue. There have been reports of BioGlue being suctioned into the aorta and impeding heart valve function when used in conjunction with an active left ventricular vent.
- Do not peel away BioGlue from an unintended site, as this could result in tissue damage.
- Do not implant BioGlue into closed anatomic locations that are in immediate proximity to nerve structures.
- Due to clinical reports[28] of ineffective sealing when BioGlue is used in the translabyrinthine approach for acoustic neuroma repairs, its use with this surgical approach is not recommended. Successful use of the product using the middle fossa or retrosigmoid approach for acoustic neuroma repair has been described in the literature and is recommended.[26]
- Published human clinical data has shown that excessive application of BioGlue in lung surgery can cause residual air space and atelectasis.[7]
- This device should be handled and disposed of in accordance with all applicable regulations including, without limitation, those pertaining to human health and safety and the environment.

UNDESIRABLE SIDE EFFECTS / ADVERSE INCIDENTS - OBSERVED and POTENTIAL

Knowledge of all possible complications of soft tissue repair surgery is necessary for physicians performing these procedures. Complications specific to these types of surgeries may occur at any time during or after the procedure.

Observed Undesirable Side Effects / Adverse Events:

Adverse events observed during the clinical studies included the following: BioGlue applied to nontargeted tissue, Failure of BioGlue to adhere, Death, Vessel rupture and hemorrhage, Cerebrospinal fluid leak, Infection, Inflammatory, Immune systemic allergic reaction, Irreversible morbidity, Ischemia, Myocardial infarction, Neurological deficit, Organ system failure, Paraplegia, Pleural Effusion, Renal Dysfunction/failure, Respiratory Dysfunction/Failure, Stroke or Cerebral Infarction, Thromboembolism, and Thrombosis.

Potential Undesirable Side Effects / Adverse Events that May Occur from the Use of BioGlue:

Complications specific to the adjunctive use of BioGlue Surgical Adhesive during soft tissue repair surgery may include, but are not limited to, the following: hypersensitivity reaction such as swelling or edema at the application site, failure of product to adhere to tissue, application of adhesive to tissue not targeted for procedure, inflammatory and immune response, allergic reaction, mineralization of tissue, local tissue necrosis, vessel obstruction, bronchial or luminal obstruction, thrombosis and thromboembolism, pulmonary emboli, injury to normal vessels or tissue, stenosis, seroma, pseudoaneurysm, and possible transmission of infectious agents from material of animal origin.

PACKAGING AND STORAGE

The BioGlue syringe and applicator tips are supplied sterile. Discard any unused material from opened or damaged product.

The BioGlue solutions are contained within a capped, double-chambered sterile syringe. Polymerized BioGlue is non-pyrogenic. Store below 25°C, but do not freeze.

ENVIRONMENTAL CONDITIONS

BioGlue Surgical Adhesive is MR safe (i.e., an item that poses no hazards in all MR environments).

DIRECTIONS FOR USE

Apply BioGlue Surgical Adhesive prophylactically or after a leak is detected.

Device Preparation

The BioGlue Surgical Adhesive Syringe delivery system consists of: syringe, syringe plunger and applicator tip.

Inside the BioGlue Syringe box there are two separate pouches. One contains the syringe and the syringe plunger, and one contains four applicator tips.

The 10mL BioGlue Syringe box includes an additional pouch containing three 12mm Spreader Tips. Visually inspect all pouches prior to use. If any breaches in the sterile barrier system are present, do not use.

1. Remove the syringe, syringe plunger, and applicator tips from their packaging. While holding the syringe upright, tap the syringe until the air bubbles in the solutions rise to the top of the syringe.

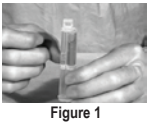


Figure 1

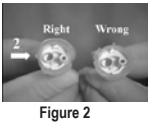


Figure 2

NOTE: Continue to hold the syringe upright during the entire assembly of the delivery system to keep the bubbles toward the top of the syringe.

2. Remove an applicator tip from its packaging and inspect the collar portion of the tip to ensure that the pointer portion is directly over the larger port. If not, rotate the locking collar on the shaft until the pointer is over the larger port. While firmly grasping the syringe, nose upward, turn the cap 90° counterclockwise and remove the cap by rocking it from side-to-side. Align the tip with the syringe using the corresponding notches on each and place the tip on the syringe.

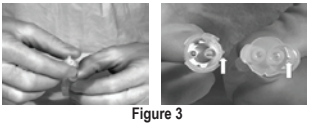


Figure 3

CAUTION: ⚠ Take care not to spill solution from the syringe during assembly.

3. Lock the applicator tip in place by pushing the tip firmly toward the syringe and rotating the tip collar 90° clockwise.

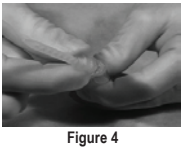


Figure 4

While keeping the syringe upright, align the small and large barrels of the syringe with the corresponding syringe plunger heads and slide the plunger into the back of the syringe until resistance is felt. The syringe delivery device is now assembled.

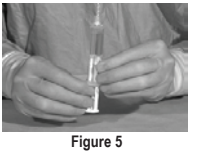


Figure 5

CAUTION: ⚠ Do not lay the assembled device on its side until all air has been purged (see next paragraph).

CAUTION: ⚠ Before using BioGlue in the procedure, the syringe must be purged of the residual air space and the applicator tip must be primed. Refer to Site Preparation, Syringe Air Space Removal and Applicator Tip Priming.

4. If using an applicator tip with a flexible extension, a desired angle may be created by bending the extension at the appropriate location to the desired angle and holding for 3-5 seconds. The angle created should be maintained for up to 5 minutes.
5. To remove occluded applicator tips, grasp the applicator tip collar, rotate the tip collar counterclockwise, and lift the tip off the syringe by rocking it side to side.

Site Preparation, Syringe Air Space Removal and Applicator Tip Priming

1. The target surgical field must be properly prepared prior to either removal of the residual air space, priming, or applying BioGlue. BioGlue works best when the target surgical field is dry. A dry surgical field can be described as a field that does not re-stain with blood within 4-5 seconds after wiping dry with a surgical sponge.

CAUTION: ⚠ Do not attempt to apply BioGlue to a field that is too wet. Application of BioGlue into a wet field may result in the failure of BioGlue to adhere.

2. The residual syringe air space must be removed prior to BioGlue application. Again, it is important to hold the assembled syringe upright to ensure that the air bubbles in the solutions are located at the top of the syringe. Purging of the air space can now be accomplished using two different methods:
   a. Compress the plunger only until the solutions are even with the top of the syringe body. Once the residual air space has been removed the syringe is ready for priming (refer to Step 3) and immediate use.
   b. Compress the plunger until both solutions can be visibly seen in the base of tip. The airspace has now been removed, but this tip is now occluded with polymerized BioGlue and will need to be changed prior to priming (refer to Step 3) and application to the target site.

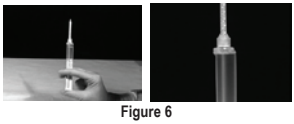


Figure 6

NOTE: Each syringe only needs to be purged of residual airspace upon its initial use.

3. Each applicator tip must be primed prior to BioGlue application. Priming ensures the BioGlue solutions are properly mixed. The surgeon should compress the plunger and expel a narrow ribbon of BioGlue approximately 3 cm long onto a sterile disposable surface (e.g., sponge, gauze, or towel).
4. The surgeon should examine the material expelled during priming and ensure that it is of uniform light yellow to amber color and that it is free from air bubbles. If this material looks colorless or contains bubbles, repeat the prime as outlined in Step 2 until the device delivers a uniform liquid with no bubbles.

CAUTION: ⚠ Avoid direct contact with material expelled during priming.

CAUTION: ⚠ If there is evidence of syringe breakage or leakage, discard the device and open/use a new one.

5. When the applicator tip has been properly primed, proceed immediately to application.

CAUTION: ⚠ BioGlue polymerizes very quickly. The surgeon must apply BioGlue immediately after priming.

Pausing between priming and application can cause polymerization of BioGlue within the applicator tip. Should this occur, replace the obstructed tip with a new tip and repeat the steps for applicator tip priming. Do not continue to apply pressure to the plunger once the tip has occluded.

General Techniques for the Use of BioGlue in Surgery[6-23,29,30]

Before using BioGlue Surgical Adhesive, surgeons should become familiar by appropriate training with the surgical techniques and variations of their specific procedures. The use of BioGlue Surgical Adhesive should be practiced with the product prior to initial use in the surgical suite.

1. The patient should be prepared and draped according to the hospital's standard procedures. Procedures such as entry of the chest or pleural space, cardiopulmonary bypass, clamping, and myocardial protection should follow the surgeon's standard techniques.
2. The tissue surrounding the surgical site can be protected from the undesired application of BioGlue Surgical Adhesive by placing moist sterile gauze pads in these areas. Directly after application, remove gauze while adhesive is still soft, wiping away excess adhesive residue from around the site.

CAUTION: ⚠ Do not use blood saving devices when suctioning excess BioGlue.

CAUTION: ⚠ Clamp and depressurize vessels prior to applying BioGlue to targeted anastomoses.

CAUTION: ⚠ Avoid suctioning BioGlue into the vessels when applying it to targeted anastomoses.

3. If BioGlue Surgical Adhesive does adhere to an undesired location, allow the adhesive to polymerize and then gently dissect the adhesive away from the unintended area with forceps and scissors. Do not attempt to peel away the BioGlue Surgical Adhesive as this could result in tissue damage at the application site.
4. For vessel repair, apply an even adhesive coating 1.2 - 3.0 mm thick for anastomosis of vessels/grafts greater than 2.5 cm in diameter; apply an even adhesive coating 0.5 - 1.0 mm for vessels/grafts less than 2.5 cm in diameter.
5. The area of adhesive application should NOT be compressed or subjected to extra pressure. BioGlue works optimally when it is allowed to polymerize without any manipulation for a full two minutes. Once the adhesive has polymerized, secure with sutures as necessary.
6. After adhesive polymerizes, trim away excess or irregular adhesive edges with scissors and pickups.

Specific Techniques for the Use of BioGlue in Aortic Dissection Surgery[6,11,13-19]

1. The dissected layers of the aorta should be initially cleared of blood and thrombus material and should be dried, to the extent possible, with surgical sponges.
2. For the distal end of the dissection repair, insert a balloon catheter into the true lumen to define the distal terminus for the application of BioGlue. In addition, the dissected layers of the aorta should be closely approximated by inserting a dilator, sponge, or catheter into the true lumen to preserve the natural architecture of the vessel.

   BioGlue should then be dispensed into the false lumen as far distally as the distal balloon catheter will allow. Filling the false lumen should proceed from distal to proximal with a spiraling out motion for smooth application. Completely fill the false lumen with BioGlue; avoid overfilling the false lumen and spilling BioGlue into the true lumen or surrounding tissue.

3. For the proximal end of the dissection repair, the dissected layers of the aorta should also be closely approximated by using a dilator, sponge, or catheter. If necessary, moist gauze pads should be placed over the aortic valve leaflets to protect them from inadvertent application of BioGlue. BioGlue should then be dispensed to fill the false lumen.

   Graft material may be sutured directly onto the tissues adhered and reinforced with BioGlue at both the proximal and distal aspects of the dissection repair. Allow BioGlue to completely polymerize without any manipulation for a full two minutes prior to suturing through the adhered tissue layers.

CAUTION: ⚠ In order to preserve the patency of the coronary lumen in the event of dissection extension, placement of a catheter into the coronary ostia prior to BioGlue application should be considered.

Use of BioGlue in Lung Surgery[6-9]

BioGlue has been shown to be effective when applied to a deflated or inflated lung.

Disposal Instructions

Discard any unused material from open or damaged product by placing it in a biohazard bin.

Summary of Safety and Clinical Performance

https://ec.europa.eu/tools/eudamed

BUDI-DI: 87723400BG35007W

Lifetime of BioGlue

BioGlue Surgical Adhesive is intended for long-term use (for more than 30 days). BioGlue degrades via proteolysis; it can be slow to resorb dependent on the quantity of adhesive applied and vascularity of the target tissue.

Reporting of Serious Incidents

Serious Incidents that occur in relation to BioGlue should be reported to the manufacturer and the competent authority of the Member State in which the patient is established. Contact information for reporting to manufacturer is below:

Artivion, Inc. 1655 Roberts Blvd, NW · Kennesaw, Georgia 30144 • USA
Phone: +1 (888) 427-9654
Fax: +1 (770) 590-3753
E-mail: fieldassurance@artivion.com

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PRODUCT INFORMATION DISCLOSURE

Handling and storage of this device by the user, as well as factors related to the patient, the diagnosis, treatment, surgical procedures, and other matters beyond manufacturer's control, may directly affect this device and the results obtained from its use.

DISCLAIMER OF WARRANTIES; LIMITS OF LIABILITY

ARTIVION DISCLAIMS ALL EXPRESS AND IMPLIED WARRANTIES WITH RESPECT TO THIS SURGICAL ADHESIVE, INCLUDING BUT NOT LIMITED TO THE EXPRESS AND IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE. IN NO EVENT SHALL ARTIVION BE LIABLE FOR INCIDENTAL OR CONSEQUENTIAL DAMAGES. In the event that such disclaimer is found invalid or unenforceable for any reason: (i) any action for breach of warranty must be commenced within one year after any such claim or cause of action accrued and (ii) the remedy for any such breach is limited to the replacement of the product.

(ru) РУССКИЙ ЯЗЫК

Инструкция по применению

ARTIVION™ | BioGlue®

www.artivion.com/eifu/bioglue

Печатная версия инструкции по применению будет предоставлена в течение семи дней после поступления запроса в службу поддержки клиентов BioGlue с использованием любого из перечисленных ниже средств связи.

Телефон: 888.427.9654 • Факс: 770.590.3753
Эл. почта: customer_service.us@artivion.com

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L09330.000 (2022-10-28)

ОБЪЯСНЕНИЕ СИМВОЛОВ

	Производитель		См. инструкцию по применению / См. электронную инструкцию по применению
	Дата производства		Внимание
	Уполномоченный представитель в ЕС		Внимание: В соответствии с Федеральным законом (США) данное устройство может продаваться только врачом или по рецепту врача
	Импортер		Апирогенно
	Медицинское изделие		Содержит биологический материал животного происхождения
	Не использовать при повреждении упаковки		Безопасно при использовании в присутствии оборудования для МРТ
	Одинарная барьерная система для стерилизации		Номер по каталогу
	Двойная барьерная система для стерилизации		Код партии
	Стерилизация оксидом этилена		Уникальный идентификатор устройства
	Радиационная стерилизация		Использовать до
	Не стерилизовать повторно		Страна производства
	Не использовать повторно		Количество
	Температурный диапазон		

ОПИСАНИЕ ПРОДУКТА

Хирургический клей BioGlue® — это двухкомпонентный хирургический клей, состоящий из растворов очищенного бычьего сывороточного альбумина и глутаральдегида. После дозирования растворы клея (в заранее определенном соотношении) смешиваются в насадке-аппликаторе, где начинается процесс образования перекрестных связей. Молекулы глутаральдегида ковалентно связывают (перекрестно) молекулы БСА друг с другом и, при нанесении, с белками ткани в месте восстановления, создавая гибкое механическое уплотнение, не зависящее от механизма свертывания крови в организме. Хирургический клей BioGlue (далее Bioglue) начинает полимеризоваться в течение 20–30 секунд, достигая заявленной прочности склеивания в течение 2-х минут. Кроме того, BioGlue прикрепляется к синтетическим материалам трансплантата за счет механического сцепления в пустотах матрицы трансплантата.

Следующие принадлежности используются для подачи хирургического клея BioGlue и продаются отдельно:

Код продукта	Описание продукта
BGAT-SY	Насадка-аппликатор
BGAT-10-SY	Насадка-удлинитель шприца — 10 см
BGAT-27-SY	Насадка-удлинитель шприца — 27 см
BGST-12	Расширительная насадка-аппликатор — 12 мм
BGST-16	Расширительная насадка-аппликатор — 16 мм
BGDTE-10	Удлинитель насадки для подачи клея — 10 см
BGDTE-27	Удлинитель насадки для подачи клея — 27 см
BGDTE-35	Удлинитель насадки для подачи клея — 35 см

Шприцы BioGlue доступны в 3-х конфигурациях — 2 мл, 5 мл и 10 мл. Каждый шприц состоит из растворов бычьего сывороточного альбумина (БСА) и глутаральдегида в соотношении 4:1 соответственно. Раствор БСА имеет янтарный цвет и является текучим. Раствор глутаральдегида прозрачный и также текучий.

Спецификация для раствора БСА — 45%-ный (соотношение веса и объема) раствор Максимальный целевой вес 45%-ного раствора БСА для каждого размера составляет: 2,71 грамма (шприц 2 мл), 4,75 грамма (шприц 5 мл) и 9,50 грамма (шприц 10 мл). Исходя из этих целевых показателей, максимальное количество материала животного происхождения, контактирующего с пациентом при использовании одного устройства, составляет 1,22 грамма (шприц 2 мл), 2,14 грамма (шприц 5 мл) и 4,23 грамма (шприц 10 мл) для каждой конфигурации.

Спецификация для раствора глутаральдегида — (соотношение веса и объема) 10%-ный раствор. Максимальный целевой вес 10%-ного раствора глутаральдегида для каждого размера составляет: 0,63 грамма (шприц 2 мл), 1,10 грамма (шприц 5 мл) и 2,16 грамма (шприц 10 мл). Исходя из этих целевых показателей, максимальное количество глутаральдегида, контактирующего с пациентом при использовании одного устройства, составляет 0,06 грамма (шприц 2 мл), 0,11 грамма (шприц 5 мл) и 0,22 грамма (шприц 10 мл) для каждой конфигурации.

ПОКАЗАНИЯ К ПРИМЕНЕНИЮ / ПРЕДУСМОТРЕННОЕ НАЗНАЧЕНИЕ

Хирургический клей BioGlue предназначен для использования в качестве дополнения к стандартным методам хирургического восстановления (таким как швы, скобы и/или пластыри) для склеивания, герметизации и/или укрепления мягких тканей. Показан к применению на следующих мягких тканях: сердечная, сосудистая, легочная и дуральная.

ЦЕЛЕВАЯ ВЫБОРКА ПАЦИЕНТОВ

Взрослые пациенты, проходящие хирургическое вмешательство, которым требуется дополнение к стандартным методам хирургического лечения для склеивания, герметизации и/или укрепления сердечных, сосудистых, дуральных и легочных тканей.

ПРЕДПОЛАГАЕМЫЕ ПОЛЬЗОВАТЕЛИ

Хирургический клей BioGlue предназначен для использования специалистами здравоохранения, например хирургами, имеющими соответствующую квалификацию.

ЭКСПЛУАТАЦИОННЫЕ ХАРАКТЕРИСТИКИ

- BioGlue достигает полной прочности склеивания в течение 2-х минут.[1]
- Хирургический клей BioGlue образует прочные ковалентные связи с тканями и механически соединяется с синтетическим материалом трансплантата. Эти прочные связи привели к тому, что BioGlue имеет зарегистрированную прочность на разрыв не менее 560 мм рт. ст. в исследованиях in vitro.[1,3,4,5]

<u>При операциях на сердце и крупных сосудах с использованием BioGlue наблюдалось:</u>

- Снижение кровотечения из линии шва анастомоза по сравнению со стандартной методикой восстановления.[12]

<u>При операциях на легких, крупных сосудах и сердце с использованием BioGlue наблюдалось:</u>

- Сокращение времени пребывания в отделении интенсивной терапии и в больнице по сравнению с использованием стандартной хирургической техники.[12, 19, 23]

<u>При устранении расслоения аорты с использованием BioGlue:</u>

- По сравнению со стандартной хирургической техникой потребовалось меньше прокладок-опор, гемостатических средств и косметических швов. [17]
- Время работы в операционной, время поперечного зажима, время остановки кровообращения, время шунтирования сократилось по сравнению с использованием стандартной хирургической техники.[18,19]
- Количество используемых тромбоцитов, плазмы и клеток крови снижено по сравнению с использованием стандартной хирургической техники.[17,19]

<u>При операциях на легких с использованием BioGlue:</u>

- BioGlue подтвердил свою эффективность для герметизации утечек воздуха при нанесении на наполненное или пустое легкое. [6,7,8,9]
- Продолжительность утечки воздуха сократилась по сравнению с использованием стандартного хирургического вмешательства.[6,8,23]

<u>При проведении дуральных процедур с использованием BioGlue:</u>

- Утечки ЦСЖ уменьшились по сравнению с использованием стандартного хирургического вмешательства.[20,21,22]

Принадлежности для хирургического клея BioGlue используются для подачи BioGlue.

КЛИНИЧЕСКИЕ ПРЕИМУЩЕСТВА

- При операциях на крупных сосудах, сердце, легких и твердой мозговой оболочке с использованием BioGlue наблюдалось:
- Показатели псевдоаневризмы были ниже по сравнению с опубликованными данными по стандартному хирургическому вмешательству.[11,14,15]
- Частота осложнений была ниже по сравнению с опубликованными данными по стандартному хирургическому вмешательству.[12, 2, 23, 18]
- Показатели смертности были ниже по сравнению с опубликованными данными по стандартному хирургическому вмешательству. [10,11,12,13,16]

ПРОТИВОПОКАЗАНИЯ

BioGlue противопоказан для использования при пластике цереброваскулярных сосудов и любых внутрипросветных областей. BioGlue не предназначен для пациентов с известной чувствительностью к материалам бычьего происхождения.

ПРЕДУПРЕЖДЕНИЯ ⚠

- Не использовать BioGlue в качестве заменителя швов или скоб при аппроксимации тканей.
- Не использовать BioGlue таким образом, чтобы он контактировал с кровотоком или препятствовал ему во время или после применения. Попадание BioGlue в кровоток может привести к локальной или эмболической обструкции сосудов.
- Не использовать BioGlue таким образом, чтобы он препятствовал циркуляции воздуха или других полостных жидкостей во время или после применения.
- Избегать контакта с нервами, глазами или другими тканями, для которых данное средство не предназначено.
- Исследование на животных[24] показало, что прямое нанесение BioGlue на открытый диафрагмальный нерв может вызвать острое повреждение нерва. Отдельное исследование на животных[25] показало, что прямое нанесение BioGlue на поверхность синоатриального узла (САУ) сердца может вызвать коагуляционный некроз, распространяющийся на миокард, который может достичь нижележащей проводящей ткани и вызвать острую, очаговую дегенерацию САУ. Более поздние испытания на животных[26,27] показали, что гель хлоргексидина глюконата может защитить френический нерв, миокард и лежащий под ним САУ от возможного повреждения при использовании BioGlue.
- При использовании BioGlue всегда надевать соответствующие средства индивидуальной защиты (например, перчатки, маску, защитную одежду и очки). Непрореагировавший глутаральдегид может вызвать раздражение глаз, носа, горла или кожи, вызвать нарушение дыхания и местный некроз тканей. Длительное воздействие непрореагировавшего глутаральдегида может вызвать патологию центральной нервной системы или сердца. В

случае контакта немедленно промыть пораженные участки водой и обратиться за медицинской помощью.

- Полимеризованный BioGlue увеличивается в объеме. При ненадлежащем использовании или неправильном применении были зарегистрированы серьезные побочные явления, связанные со сдавливанием соседних анатомических структур. BioGlue следует использовать только при условии полной визуализации места нанесения, правильного грунтования для достижения оптимальной вязкости и использования минимального количества. См. разделы *«Показания к применению/Предусмотренное назначение»* и *«Способ применения»* в этом листке-вкладыше.
- Свести к минимуму использование BioGlue у пациентов с нарушением обмена кальция (например, хроническая почечная недостаточность, гиперпаратиреоз). Обработанные глутаральдегидом ткани имеют повышенную склонность к минерализации. Лабораторные эксперименты показали, что непрореагировавший глутаральдегид может оказывать мутагенное действие.
- Не использовать BioGlue при наличии инфекции и использовать с осторожностью на загрязненных участках тела.
- Соблюдать осторожность при повторном использовании BioGlue у одного и того же пациента. При контакте с BioGlue возможны реакции гиперчувствительности. У животных наблюдалась сенсибилизация.
- BioGlue содержит материал животного происхождения, который потенциально может передавать инфекционные агенты.
- Применение BioGlue у беременных/кормящих женщин не изучалось.
- Шприц и принадлежности BioGlue пригодны только для одноразового использования, и не должны применяться для нескольких пациентов.
- Применение BioGlue у педиатрических пациентов не изучалось. BioGlue не следует наносить на ткань по окружности, это может не позволить ткани расти или расширяться.
- Пригодность к использованию BioGlue для лечения бронхоплевральных фистул (БПФ) или мест утечки лимфы не подтверждена достаточным количеством данных.
- При использовании BioGlue в сочетании с любым другим материалом необходимо тщательно изучить инструкции к обоим продуктам и соблюдать их.

МЕРЫ ПРЕДОСТОРОЖНОСТИ ⚠

- Рекомендуется поддерживать хирургические перчатки, стерильные марлевые салфетки/полотенца и хирургические инструменты во влажном состоянии, чтобы минимизировать вероятность случайного прилипания BioGlue к этим поверхностям.
- Шприц, насадки-аппликаторы, расширительные насадки и насадки-удлинители шприца BioGlue должны использоваться только для одного пациента. Не стерилизовать повторно.
- Не использовать, если упаковка была вскрыта или повреждена.
- Проявлять осторожность, чтобы не пролить содержимое шприца.
- Не нажимать на поршень, прикрепляя его к шприцу.
- Не наносить BioGlue на слишком влажное операционное поле. Это может привести к плохой адгезии.
- Избегать контакта тканей с материалом, выходящим из аппликатора во время грунтования.
- BioGlue быстро полимеризуется. Грунтование должно выполняться быстро, после чего следует сразу же нанести BioGlue. Пауза между грунтованием и нанесением клея может привести к полимеризации в насадке-аппликаторе.
- Не использовать кровосберегающие устройства при отсасывании излишков BioGlue из операционного поля.
- Перед нанесением BioGlue на целевые анастомозы зажать сосуды и снизить в них давление.
- Чтобы предотвратить попадание BioGlue в сердечно-сосудистую систему, избегать любого отрицательного давления во время нанесения и полимеризации BioGlue. Например, перед применением BioGlue следует отключить катетер для дренажа левого желудочка. Сообщалось, что при использовании в сочетании с активным катетером для дренажа левого желудочка BioGlue втягивается в аорту, вызывая нарушение функции сердечного клапана.
- Не удалять BioGlue при случайном попадании на ткани, так как это может привести к их повреждению.
- Не имплантировать BioGlue в закрытые анатомические участки, находящиеся в непосредственной близости от структур нервной системы.
- Ввиду клинических отчетов[28] о неэффективности герметизации с использованием BioGlue при транслабиринтном доступе для лечения акустической невриномы, не рекомендуется использовать его при данном хирургическом подходе. Рекомендуется описанное в литературе успешное применение продукта для лечения акустической невриномы при доступе через среднюю черепную ямку или ретросигмоидном доступе.[26]
- Опубликованные клинические данные людей показали, что чрезмерное применение BioGlue в хирургии легких может вызвать образование остаточного воздушного пространства и ателектаз.[7]
- Данное устройство следует использовать и утилизировать в соответствии со всеми применимыми правилами, в том числе правилами, касающимися здоровья и безопасности человека и окружающей среды.

НЕЖЕЛАТЕЛЬНЫЕ ПОБОЧНЫЕ ЭФФЕКТЫ / НЕЖЕЛАТЕЛЬНЫЕ ЯВЛЕНИЯ — НАБЛЮДАЕМЫЕ И ПОТЕНЦИАЛЬНЫЕ

Врачи, выполняющие эти процедуры, должны знать обо всех возможных осложнениях операции по восстановлению мягких тканей. Осложнения, характерные для этих видов операций, могут возникнуть как во время, так и после процедуры.

Наблюдаемые нежелательные побочные эффекты / нежелательные явления:

В ходе клинических исследований наблюдались следующие нежелательные явления: нанесение BioGlue на нецелевую ткань, неспособность BioGlue к адгезии, смерть, разрыв сосуда и кровоизлияние, утечка спинномозговой жидкости, инфекция, воспаление, иммунная системная аллергическая реакция, необратимые клинические проявления заболевания, ишемия, инфаркт миокарда, неврологический дефицит, отказ системы органов, параплегия, плевральная эффузия, почечная дисфункция/отказ, дыхательная дисфункция/отказ, инсульт или церебральный инфаркт, тромбоэмболия и тромбоз

Потенциальные нежелательные побочные эффекты / нежелательные явления, которые могут возникнуть при использовании BioGlue:

Осложнения, характерные для дополнительного использования хирургического клея BioGlue во время операций по восстановлению мягких тканей, могут включать, помимо прочего, следующее: реакция гиперчувствительности, такая как припухлость или отек в месте применения, неспособность продукта приклеиться к ткани, применение клея на ткани, не предназначенной для процедуры, воспалительный и иммунный ответ, аллергическая реакция, минерализация ткани, местный некроз ткани, обструкция сосудов, обструкция бронхов или просвета, тромбоз и тромбоэмболия, легочная эмболия, повреждение нормальных сосудов или тканей, стеноз, серома, псевдоаневризма и возможная передача инфекционных агентов из материала животного происхождения.

УПАКОВКА И ХРАНЕНИЕ

Шприц BioGlue и насадки-аппликаторы поставляются стерильными. Неиспользованный материал из вскрытого или поврежденного изделия следует выбросить.

Растворы BioGlue содержатся в закупоренном двухкамерном стерильном шприце. Полимеризованный BioGlue является непирогенным. Хранить при температуре ниже 25 °C, но не замораживать.

ОКРУЖАЮЩИЕ УСЛОВИЯ

Хирургический клей BioGlue является безопасным для использования в присутствии оборудования для МРТ (т.е. не представляет опасности во всех средах МР).

СПОСОБ ПРИМЕНЕНИЯ

Наносить хирургический клей BioGlue в качестве профилактики или после обнаружения утечки.

Подготовка устройства

Шприцевая система нанесения хирургического клея BioGlue состоит из: шприца, поршня и насадки-аппликатора.

В коробке для шприца BioGlue находятся два отдельных пакета. В одном содержится шприц и поршень, а в другом — четыре насадки-аппликатора.

В коробку для шприца BioGlue объемом 10 мл входит дополнительный пакет, содержащий три 12-миллиметровых расширительных насадки. Перед использованием необходимо осмотреть все пакеты. Не использовать изделие при обнаружении каких-либо нарушений барьерной системы для стерилизации.

1. Извлечь шприц, поршень и насадки-аппликаторы из упаковки. Держа шприц вертикально, постукивать по нему, пока пузырьки воздуха в растворах не поднимутся к верху шприца.

Рисунок 1

Рисунок 2

ПРИМЕЧАНИЕ: удерживать шприц в вертикальном положении на протяжении всей сборки шприцевой системы, чтобы пузырьки поднимались к верху шприца.

2. Извлечь насадку-аппликатор из упаковки и осмотреть кольцевую часть насадки, чтобы убедиться, что указатель находится непосредственно над большим отверстием.

Если это не так, повернуть блокирующее кольцо на стержне, пока указатель не окажется над большим отверстием. Крепко удерживая шприц носиком вверх, повернуть колпачок на 90° против часовой стрелки и снять его, раскачивая из стороны в сторону. Совместить насадку со шприцем, используя соответствующие выемки на них, и надеть насадку на шприц.

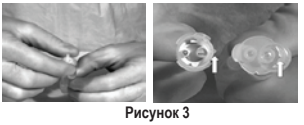

Рисунок 3

ВНИМАНИЕ: ⚠ Следить за тем, чтобы не пролить раствор из шприца во время сборки.

3. Зафиксировать насадку-аппликатор на месте, плотно прижав ее к шприцу и повернув кольцевую часть насадки на 90° по часовой стрелке.

Рисунок 4

Удерживая шприц в вертикальном положении, совместить малый и большой цилиндры шприца с соответствующими головками поршня и вставить поршень в заднюю часть шприца до появления сопротивления. Шприцевое устройство подачи хирургического клея собрано.

Рисунок 5

ВНИМАНИЕ: ⚠ Не класть собранное устройство на бок, пока не будет удален весь воздух (см. следующий пункт).

ВНИМАНИЕ: ⚠ Перед использованием BioGlue на пациенте необходимо удалить из шприца остатки воздуха и загрунтовать насадку-аппликатор. См. «Подготовка операционного поля, удаление воздуха из шприца и грунтование насадки-аппликатора».

4. При использовании насадки-аппликатора с гибким удлинителем необходимый угол можно создать, согнув удлинитель в соответствующем месте до нужного угла и удерживая его в течение 3–5 секунд. Созданный угол должен сохраняться в течение 5 минут.
5. Для удаления закупоренных насадок-аппликаторов взяться за манжету насадки-аппликатора, повернуть кольцевую часть против часовой стрелки и снять насадку со шприца, расшатывая ее из стороны в сторону.

Подготовка операционного поля, удаление воздуха из шприца и грунтование насадки-аппликатора

1. Перед удалением остатков воздуха, заправкой или нанесением BioGlue необходимо надлежащим образом подготовить целевое операционное поле. BioGlue лучше всего работает на сухом операционном поле. Сухое операционное поле можно охарактеризовать как поле, которое не окрашивается снова кровью в течение 4–5 секунд после вытирания насухо хирургической губкой.

ВНИМАНИЕ: ⚠ Не следует наносить BioGlue на слишком влажное поле. Нанесение BioGlue на влажное поле может привести к нарушению адгезии BioGlue.

2. Перед нанесением BioGlue необходимо удалить остатки воздуха из шприца. Опять же, важно держать собранный шприц вертикально, чтобы пузырьки воздуха в растворах находились в верхней части шприца. Теперь удалить воздух можно двумя различными способами:
   a. Нажимать на поршень до тех пор, пока растворы не сравняются с верхней частью корпуса шприца. После удаления остатков воздуха шприц готов к грунтованию (см. шаг 3) и немедленному использованию.
   b. Нажимать на поршень до тех пор, пока оба раствора не будут видны в основании насадки. Воздушное пространство удалено, но насадка теперь закупорена полимеризованным BioGlue, и ее необходимо заменить перед грунтованием (см. шаг 3) и нанесением на целевой участок.

Рисунок 6

ПРИМЕЧАНИЕ: Каждый шприц необходимо очищать от остатков воздуха только при первом использовании.

3. Перед нанесением BioGlue необходимо загрунтовать каждую насадку-аппликатор. Грунтование обеспечивает правильное смешивание растворов BioGlue. Хирург должен нажать на поршень и выдавить узкую полосу клея BioGlue длиной около 3 см на стерильный расходный материал (например, губку, марлю или полотенце).
4. Хирург должен осмотреть выдавленный во время грунтования материал и убедиться, что он имеет однородный цвет от светло-желтого до янтарного и не содержит пузырьков воздуха. Если этот материал выглядит бесцветным или содержит пузырьки, необходимо повторять грунтование, как описано в шаге 2, пока устройство не начнет выдавать однородную жидкость без пузырьков.

ВНИМАНИЕ: ⚠ Следует избегать прямого контакта с материалом, выдавливаемым при грунтовании.

ВНИМАНИЕ: ⚠ При наличии признаков поломки шприца или утечки, необходимо утилизировать данное устройство и открыть/использовать новое.

5. Как только насадка-аппликатор будет надлежащим образом загрунтована, следует немедленно приступить к нанесению препарата.

ВНИМАНИЕ: ⚠ BioGlue очень быстро полимеризуется. Хирург должен наносить BioGlue сразу после грунтования.

Пауза между грунтованием и нанесением клея может привести к полимеризации BioGlue в насадке-аппликаторе. В этом случае необходимо заменить закупоренную насадку и повторить шаги по грунтованию насадки-аппликатора. При закупоривании насадки следует прекратить давление на поршень.

Общая техника использования BioGlue в хирургии[6-23,29,30]

Перед использованием хирургического клея BioGlue хирурги должны пройти соответствующее обучение для ознакомления с хирургическими техниками и вариациями их специфических процедур. Перед первым применением необходимо отработать использование хирургического клея BioGlue в операционном блоке.

1. Пациент должен быть подготовлен и покрыт простынями в соответствии со стандартными больничными процедурами. Такие процедуры, как вход в грудную клетку или плевральную полость, сердечно-легочное шунтирование, наложение зажимов и защита миокарда, должны выполняться стандартными хирургическими методами.
2. Ткани, окружающие операционное поле, можно защитить от случайного нанесения хирургического клея BioGlue, наложив на эти области влажные стерильные марлевые салфетки. Сразу после нанесения снять марлю, пока клей еще мягкий, и стереть излишки клея вокруг места нанесения.

ВНИМАНИЕ: ⚠ Не использовать кровосберегающие устройства при отсасывании излишков BioGlue.

ВНИМАНИЕ: ⚠ Перед нанесением BioGlue на целевые анастомозы зажать сосуды и снизить в них давление.

ВНИМАНИЕ: ⚠ Избегать всасывания BioGlue в сосуды при нанесении его на целевые анастомозы.

3. Если хирургический клей BioGlue прилип к нежелательному участку, необходимо дать клею полимеризоваться, а затем аккуратно удалить его с этого участка с помощью щипцов и ножниц. Не следует пытаться оторвать хирургический клей BioGlue, так как это может привести к повреждению тканей в месте применения.
4. Для восстановления сосудов нанести равномерный слой клея толщиной 1,2–3,0 мм для анастомоза сосудов/трансплантатов диаметром более 2,5 см; при диаметре сосудов/трансплантатов менее 2,5 см нанести равномерный слой клея толщиной 0,5–1,0 мм.
5. Область нанесения клея НЕ должна сжиматься или подвергаться дополнительному давлению. BioGlue работает оптимально, когда ему дают полимеризоваться без каких-либо манипуляций в течение двух минут. После

полимеризации клея при необходимости закрепить его швами.

6. После полимеризации обрезать излишки или неровные края клея с помощью ножниц и пинцета.

Особые техники использования BioGlue в хирургии расслаивающей аневризмы аорты[6,11,13-19]

1. Расслоенные стенки аорты сначала нужно очистить от крови и тромбов и по возможности просушить хирургическими губками.
2. Для восстановления дистального конца расслоения ввести баллонный катетер в истинный просвет, чтобы определить дистальный конец для нанесения BioGlue. Кроме того, расслоенные стенки аорты должны быть тщательно сведены путем введения дилататора, губки или катетера в истинный просвет для сохранения естественной архитектуры сосуда.

   Затем в ложный просвет следует ввести BioGlue настолько дистально, насколько это позволяет дистальный баллонный катетер. Заполнение ложного просвета должно происходить от дистального к проксимальному участку спиралевидными движениями для плавного нанесения. Полностью заполнить ложный просвет клеем BioGlue; избегать переполнения ложного просвета и проливания BioGlue в истинный просвет или окружающие ткани.

3. На проксимальном конце расслоенные стенки аорты следует также тщательно свести с помощью дилататора, губки или катетера. При необходимости на створки аортального клапана следует положить влажные марлевые салфетки, чтобы защитить их от случайного нанесения BioGlue. Затем следует нанести BioGlue, чтобы заполнить ложный просвет.

   Материал трансплантата можно пришивать непосредственно к тканям, склеенным и укрепленным клеем BioGlue, как в проксимальной, так и в дистальной части восстановления рассечения. Перед наложением швов на склеенные слои тканей BioGlue должен полностью полимеризоваться без каких-либо манипуляций в течение двух минут.

ВНИМАНИЕ: ⚠ Для сохранения проходимости коронарного просвета в случае расширения диссекции следует рассмотреть возможность установки катетера в коронарное устье перед применением BioGlue.

Использование BioGlue в хирургии легких[6-9]

BioGlue подтвердил свою эффективность при нанесении на наполненное или пустое легкое.

Инструкции по утилизации

Неиспользованный материал из вскрытого или поврежденного изделия следует выбросить, поместив его в контейнер для биологически опасных отходов.

Сводное резюме по безопасности и клинической эффективности

https://ec.europa.eu/tools/eudamed
BUDI-DI: 87723400BG35007W

Срок службы BioGlue

Хирургический клей BioGlue предназначен для длительного использования (более 30 дней). BioGlue разрушается в результате протеолиза; рассасывание может происходить медленно и зависит от количества нанесенного клея и сосудистости целевой ткани.

Сообщение о серьезных инцидентах

О серьезных инцидентах, связанных с BioGlue, следует сообщать производителю и компетентному органу государства-члена ЕС, в котором находится пациент. Контактная информация для сообщения производителю приведена ниже:

Artivion, Inc. 1655 Roberts Blvd, NW
Kennesaw, Georgia 30144 • USA
Телефон: +1 (888) 427-9654
Факс: +1 (770) 590-3753
:Эл. почта: fieldassurance@artivion.com

ИСПОЛЬЗОВАННАЯ ЛИТЕРАТУРА

Ссылки на информацию, содержащуюся в данном листке-вкладыше, предоставляются по запросу.

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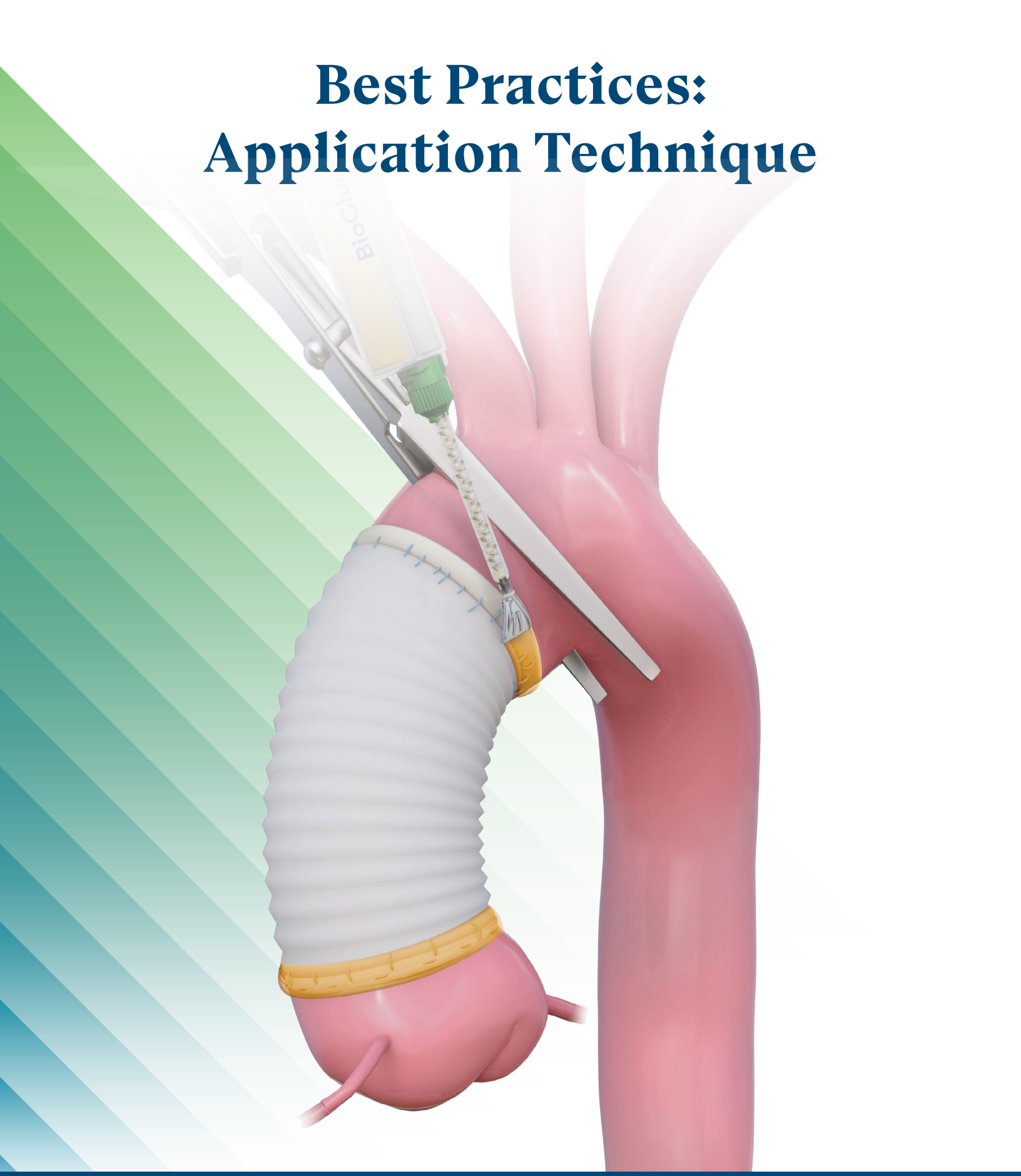
РАСКРЫТИЕ ИНФОРМАЦИИ О ПРОДУКТЕ

Способ обращения с данным устройством и его хранение пользователем, а также факторы, относящиеся к пациенту, диагностике, лечению, хирургическим процедурам и другим вопросам, не зависящим от производителя, могут оказывать непосредственное влияние на это устройство и результаты, полученные при его использовании.

ОТКАЗ ОТ ПРЕДОСТАВЛЕНИЯ ГАРАНТИЙ; ОГРАНИЧЕНИЕ ОТВЕТСТВЕННОСТИ

КОМПАНИЯ ARTIVION НЕ БЕРЕТ НА СЕБЯ НИКАКИХ ОБЯЗАТЕЛЬСТВ В ОТНОШЕНИИ ЯВНО ВЫРАЖЕННЫХ И ПОДРАЗУМЕВАЕМЫХ ГАРАНТИЙ ОТНОСИТЕЛЬНО ДАННОГО ХИРУРГИЧЕСКОГО КЛЕЯ, ВКЛЮЧАЯ ЯВНО ВЫРАЖЕННЫЕ И ПОДРАЗУМЕВАЕМЫЕ ГАРАНТИИ ТОВАРНОГО КАЧЕСТВА И СООТВЕТСТВИЯ НАЗНАЧЕНИЮ. КОМПАНИЯ ARTIVION НИ ПРИ КАКИХ ОБСТОЯТЕЛЬСТВАХ НЕ НЕСЕТ ОТВЕТСТВЕННОСТИ ЗА СЛУЧАЙНЫЕ ИЛИ КОСВЕННЫЕ УБЫТКИ. В случае, если такой отказ от ответственности по какой-либо причине будет признан недействительным или не имеющим законной силы: (i) любой иск о нарушении гарантии должен быть подан в течение одного года с момента возникновения претензии или основания для иска, и (ii) правовая защита от любого такого нарушения ограничивается заменой товара.

Best Practices: Application Technique



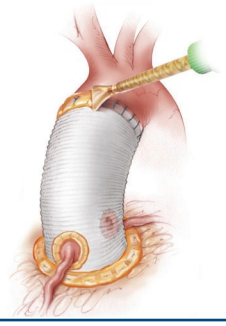
ARTIVION™ | BioGlue® Surgical Adhesive

BioGlue has been used in more than 2
continues to provide significant benefits for mo

Proper application of BioGlue results in effective hemostasis as well as tissue sealing and rei

Aortic Valve Replacement

Full Root: Proximal and distal anastomoses + 2 coronary buttons
Subcoronary: Aortotomy suture line

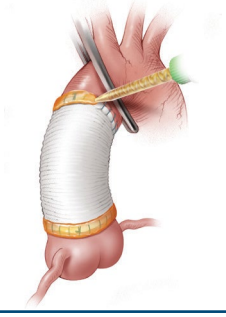


Technique: Apply a thin layer using the spreader or standard applicator tip to seal anastomoses and suture lines. Standard applicator tip allows pinpoint application when sealing coronary buttons.

"I tend to use a little bit of BioGlue in some of the older patients for straightforward AVR's, it works fantastic." – Joseph Bavaria, M.D.[1]

Aortic Aneurysm Repair

Thoracic: Proximal and distal anastomoses
Thoracoabdominal: Proximal and distal anastomoses + 1 or more side branches to organs

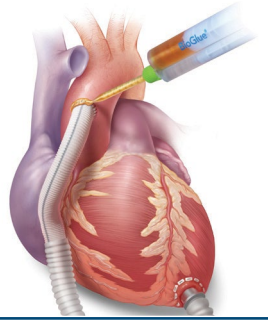


Technique: Apply a thin layer to all anastomoses using the spreader or standard applicator tip. Application to all areas of suture can reinforce tissue and aid in the prevention of post-op bleeding.[6]

"The surgeons in our institution consider BioGlue, when applied appropriately and without excess, to be effective in its function as a hemostat, tissue strengthener and adherent." – Mark O'Brien, M.D., et al.[2]

Ventricular Assist Device Implantation

Aorta: Aortic cannula suture line
Pulmonary: Pulmonary artery cannula suture line



Technique: Use the standard applicator tip to apply a thin layer to outflow cannulation site to seal the suture lines and reinforce friable tissue.

"[BioGlue] is a useful operative adjunct to aid in hemostasis and to provide structural integrity for fragile tissues." – Kenton Zehr, M.D.[3]

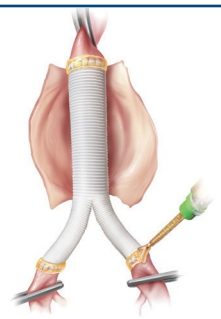
Surgical technique is at the discretion of the surgeon. Variations in technique and practices will inevitably and appropriately occur when clinicians

2.5 million procedures* since 1998 and ore than just dissection repair.

inforcement. BioGlue's hydrogel technology will remain flexible in a moist environment.

Abdominal Aortic Aneurysm Repair

Abdominal aorta: Proximal and two distal anastomoses + 1 or more side branches to organs if involved

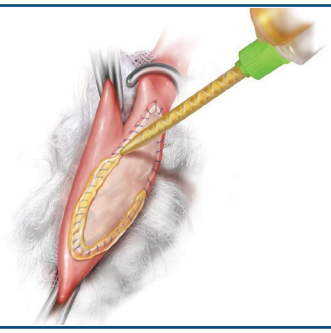


Technique: Apply a thin layer using the spreader or standard applicator tip to all anastomoses to seal and reinforce calcified tissue. Judicious use on all anastomoses can aid in the prevention of post operative bleeding.[6]

"Use of [BioGlue] helped to facilitate a minimal reliance on blood products and a low mortality rate." – John Fehrenbacher, M.D.[4]

Carotid Endarterectomy

Carotid artery: Patch-to-tissue suture line

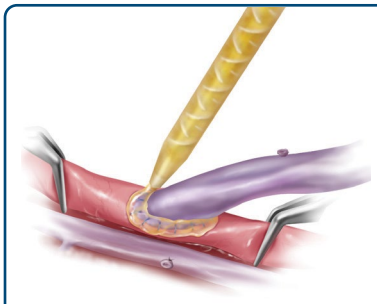


Technique: Apply a thin layer to suture line using the standard applicator tip to prevent suture hole bleeding. BioGlue when applied correctly will remain flexible and pliable in the body.

"Immediate anastomotic hemostasis was found to be statistically superior in the BioGlue group when compared with the standard surgery control." – Joseph Coselli, M.D., et al.[5]

Peripheral Bypass / AV Access

AV access: Proximal and distal anastomoses
Peripheral bypass: Proximal and distal anastomoses



Technique: Apply a thin layer to the suture line using the standard applicator tip to prevent suture hole bleeding and reinforce fragile end-to-end and end-to-side anastomoses.

"Use of BioGlue reinforces friable tissue, facilitating anastomotic repair when tissues are fragile because of age or disease state."
– Joseph Coselli, M.D., et al.[5]

take into account the needs of the individual patients, available resources, and limitations unique to an institution or type of practice.

Catalogue #	Product	Contains
BG3510-5-US	Syringe 10mL 5-Pack Kit	Five single packs – Each contains one 10mL syringe and syringe plunger, four standard syringe tips
BG3515-5-US	Syringe 5mL 5-Pack Kit	Five single packs – Each contains one 5mL syringe and syringe plunger, and four standard syringe tips
BGAT-SY	Syringe Applicator Tip	Ten single packs – Each contains four standard syringe tips
BGAT-10-SY	Syringe 10cm Applicator Tip	Ten single packs – Each contains four 10cm syringe tips
BGAT-27-SY	Syringe 27cm Applicator Tip	Ten single packs – Each contains four 27cm syringe tips
BGST-12	Syringe 12mm Spreader Tip	Ten single packs – Each contains three 12mm spreader tips
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*Data on file.

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Phone: 888-427-9654 | Fax: 770-590-3573 | E-mail: inquiries@artivion.com
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Syringe Assembly Procedure

Safe | Simple | Effective

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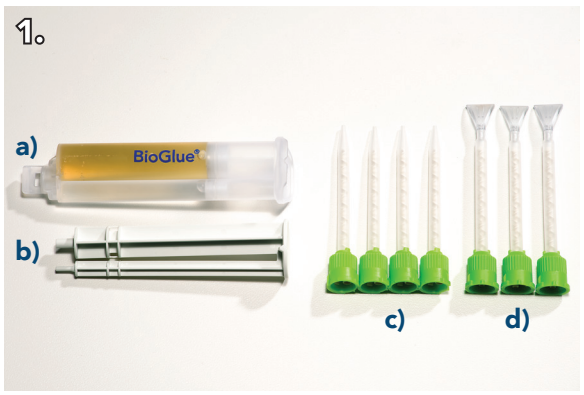
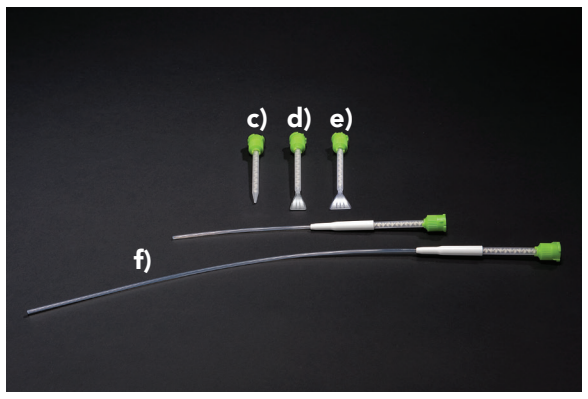
Surgical Adhesive



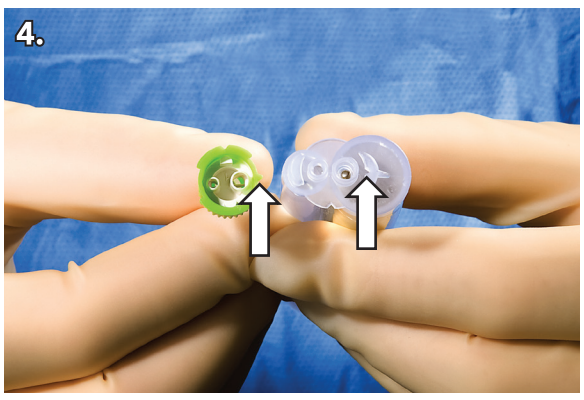


1. **System Components:**
   a) Pre-filled BioGlue Syringe
   b) Syringe Plunger
   c) Syringe Applicator Tips
   d) 12mm Spreader Tips
   e) 16mm Spreader Tips
   f) Applicator Tips with Flexible Extensions (10cm and 27cm)

NOTE: Hold syringe upright during assembly.

2. Hold syringe upright and tap until air bubbles rise to the top.

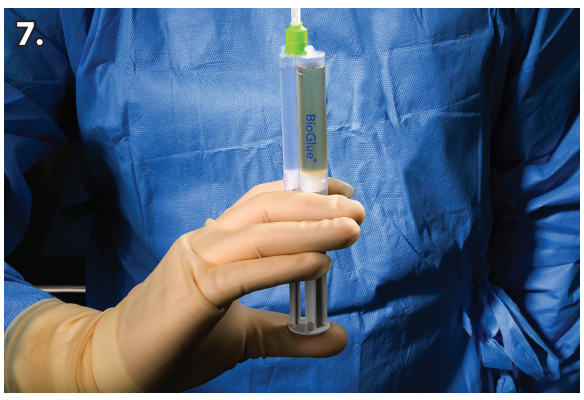
3. Remove cap by twisting 90° counter-clockwise and gently lift it from syringe.



4. Align the triangular notch on the collar of the applicator tip with the corresponding notch on the syringe nose.

5. Seat the tip firmly on syringe and rotate collar 90° clockwise to lock in place.

6. Align the barrels of the syringe with the plunger heads and slide the plunger into the syringe until resistance is felt.



7. Remove the residual air space using one of two methods:
   a) Compress the plunger only until the solutions are even with top of the syringe body. The syringe is now ready for priming and immediate use.
   b) Compress the plunger until both solutions can be visibly seen in the base of the tip. Change the tip prior to priming and use.

Keys To Success

1. **De-Air** remove all air from the syringe.
2. **Dry** the target site (by suction and/or gauze).
3. **Prime** the syringe.
4. **Apply** a thin layer in a slow and steady manner.
5. **Wait** 2 minutes for full strength.

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See Instruction for Use for Indications, Contraindications, Warnings, Precautions and other important information.

BioGlue Syringe Delivery System

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BG3502-5-US	Syringe 2mL 5-Pack Kit	Five single packs – Each contains one 2mL syringe and syringe plunger, and four standard syringe tips
BGAT-SY	Syringe Applicator Tip	Ten single packs – Each contains four standard syringe tips
BGAT-10-SY	Syringe 10cm Applicator Tip	Ten single packs – Each contains four 10cm syringe tips
BGAT-27-SY	Syringe 27cm Applicator Tip	Ten single packs – Each contains four 27cm syringe tips
BGAT-10-SY	Syringe 10cm Applicator Tip	Ten single packs – Each contains four 10cm syringe tips
BGST-12	Syringe 12mm Spreader Tip	Ten single packs – Each contains three 12mm spreader tips
BGST-16	Syringe 16mm Spreader Tip	Ten single packs – Each contains three 16mm spreader tips

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MLENG0161.004 (2022-07)

MECHANICAL
HEART VALVES

BICARBON™ FAMILY

Distinguished details
make the dynamic
difference

CORCYM
WE TAKE LIFE TO HEART

BICARBON™ FAMILY

Many options for many benefits[1,2]

CORCYM Bicarbon™ mechanical heart valves have been specifically designed to offer an advanced solution to patients undergoing cardiac valve replacement.

Featuring many distinguished details, Bicarbon valves provide favorable hemodynamic performance[3,4] combined with proven safety and durability.* The benefits of its innovative and distinguished design are reflected in the desirable clinical outcomes[2,5]** reported in scientific literature across over 25 years of clinical use.

Bicarbon mechanical valves feature the exclusive CORCYM Carbofilm™ coating technology which favors both hemo and biocompatibility.[6]

Innovative design,[2] innovative choice of materials and a proven track record of positive clinical results make this valve an advanced solution backed by compelling long term data.[2,5]*

*The Bicarbon range boasts trusted clinical results[2,5]** in over 25 years of clinical use. The distinguished design features offer a favorable hemodynamic performance,[3,4] optimal thromboresistance,[7,8] ease of implant and proven safety and durability*.*

* Based on CORCYM post-market surveillance, valve structural failure is expected to occur less than 1 time per 1000000 device population.

** Based on CORCYM post-market surveillance, valve structural failure is expected to occur less than 1 time per 1000000 device population, while valve-related thromboembolic events are expected to occur between 0.1 and 1 times per 100000 device population.

1. *Celiento et al., Single center experience with the Sorin Bicarbon prosthesis: A 17-year clinical follow-up, J Thorac Cardiovasc Surg, 148:2039-44, 2014.*
2. *Azarnoush et al., the Sorin Bicarbon over 15 years clinical outcomes: multicentre experience in 1704 patients, Eur J Cardio-thoracic Surg; 38:759—66, 2010.*
3. *Reyes et al., Results of aortic valve replacement with the supra-annular Sorin Bicarbon Overline prosthesis, J Heart Valve Dis, 21 (3): 358-63, 2012.*
4. *Badano et al., Normal echocardiographivc characteristics of the Sorin Bicarbon bileaflet prosthetic heart valve in the mitral and aortic positions, J Am Soc Echocardiogr 10: 632- 43, 1997.*
5. *Misawa et al., Fifteen-year experience with the Bicarbon heart valve prosthesis in a single center, J Cardiothorac Surg, 10: 89, 2015.*
6. *Vallana et al., Carbofilm: Present and Future Applications in Biomedical Devices, Ceramics International 19 (1993) 169-179.*
7. *Torella et al., LOWERing the INtensity of oral anticoaGulant Therapy in patients with bileaflet mechanical aortic valve replacement: Results from the "LOWERING-IT" Trial, Am Heart J; 160:171-8, 2010.*
8. *Falk et al., 2017 ESC/EACTS Guidelines for the management of valvular heart disease. The Task Force for the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS), European Journal of Cardio-Thoracic Surgery 52 (2017) 616–664.*

Technical claims are supported by CORCYM data on file.

Details make the difference

Hemodynamics

Thromboresistance

Safety and Durability

Clinical outcomes

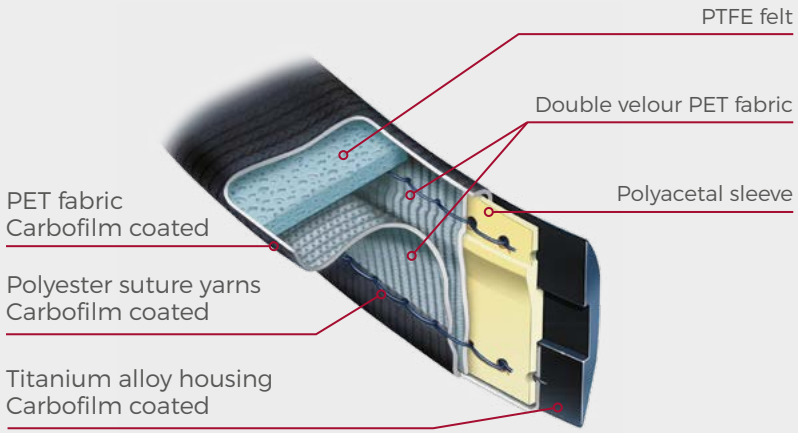
Details make the difference: Hemodynamics[1,2]

Bicarbon’s distinguished details make the difference when it comes to hemodynamic performance[1,2]

Careful choice of materials.

CORCYM Bicarbon is a unique valve featuring a Titanium housing coated with Carbofilm. Titanium is a highly biocompatible material with greater structural stability than the commonly used Pyrolite Carbon. This allows for a slimmer housing, increasing the area available for blood flow.[3]

The CORCYM proprietary Carbofilm coating is applied to both the valve's Titanium housing and the sewing cuff. The coating favors hemocompatibility, minimizing the risk for pannus formation* and favoring a gentle tissue ingrowth.[3,4]

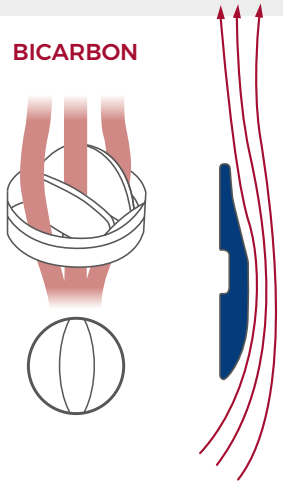


* Based on CORCYM post-market surveillance, valve-related pannus formation is expected to occur between 0.1 and 1 times per 100000 device population.

Technical claims are supported by CORCYM data on file.

Innovative Design

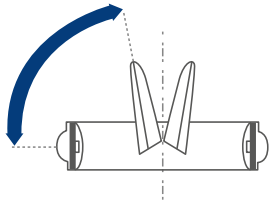
Not only a careful choice of materials but also an innovative design are key to Bicarbon's hemodynamic performance.[1,2]

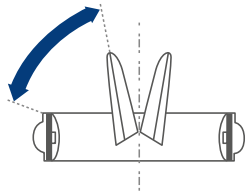


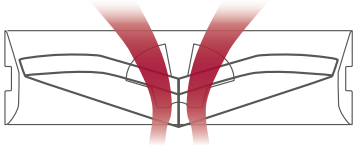
Bicarbon is a unique mechanical heart valve featuring curved leaflets specifically engineered to achieve an even flow distribution downstream.[3] This leads to several benefits to the patien:[1,3]

- low turbulence which prevents blood stasis and thus the risk for thrombus formation
- low pressure gradients for favorable hemodynamic performance
- reduced energy loss for an efficient functioning and beneficial cardiac workload.

The 80-degree opening angle, in combination with curved leaflets has been specifically established to minimize turbulence, while the short travel arc contributes to low regurgitation levels and low energy loss.[1,3]







The unique two-open-chimney design ensures an effective passive washing of the hinges even when the valve is closed, avoiding blood stasis and hemolysis at the same time.[3,5]

Technical claims are supported by CORCYM data on file.

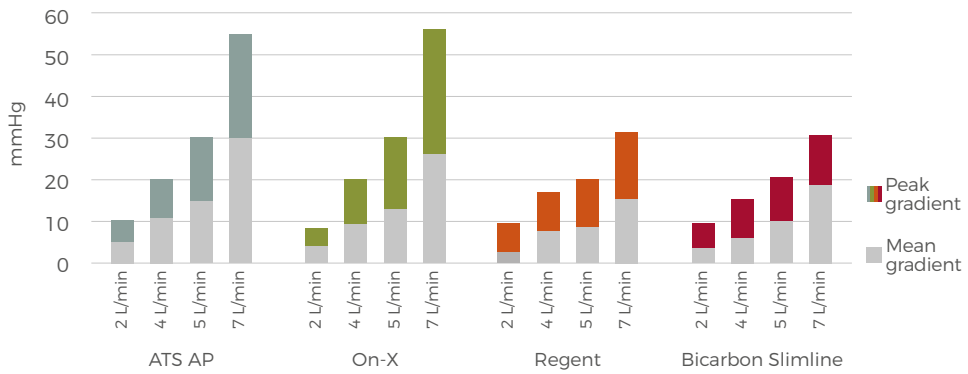
The favorable hemodynamic performance of Bicarbon valves is well proven in the published scientific literature.[1,2]

In vitro comparisons[1] with other commercially available valves have shown that Bicarbon are among the best performing valves with respect to all the relevant parameters:

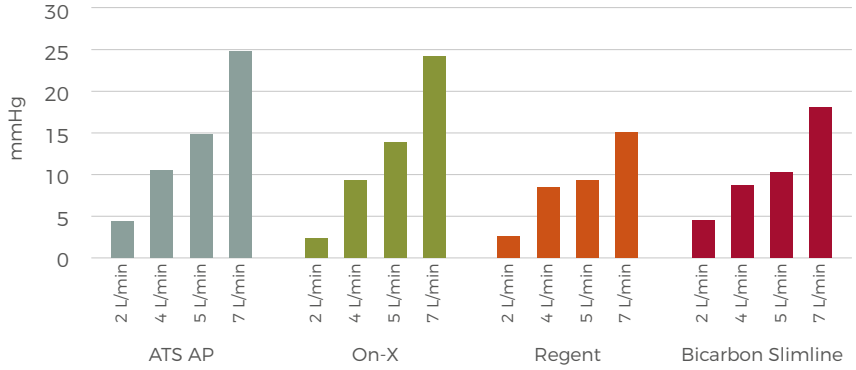
- pressure gradients
- leakage volume
- energy loss
- velocity profiles
- shear stress distribution

This is confirmed in small aortic annuli, even when compared with valves specifically designed to improve hemodynamic performance.[6,7,8]

Mean and peak pressure gradients at 70 bpm (mmHg)*



Energy loss at 70 bpm (%)*[6]



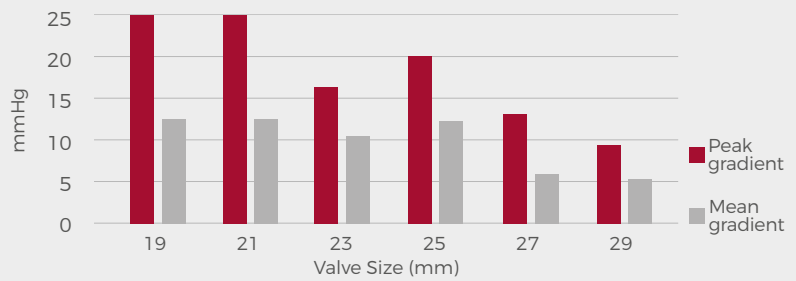
* Test performed with Sheffield pulse duplicator. Valves fitting a 21 mm diameter valve holder.

Technical claims are supported by CORCYM data on file.

The hydrodynamic efficiency of Bicarbon valves is reflected by the favorable hemodynamic results reported in the published in-vivo evaluations.[9]

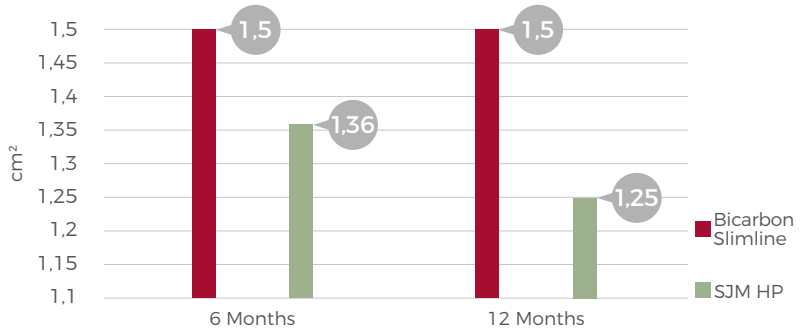
Peak and Mean Pressure Gradients*

IN VIVO AORTIC POSITION

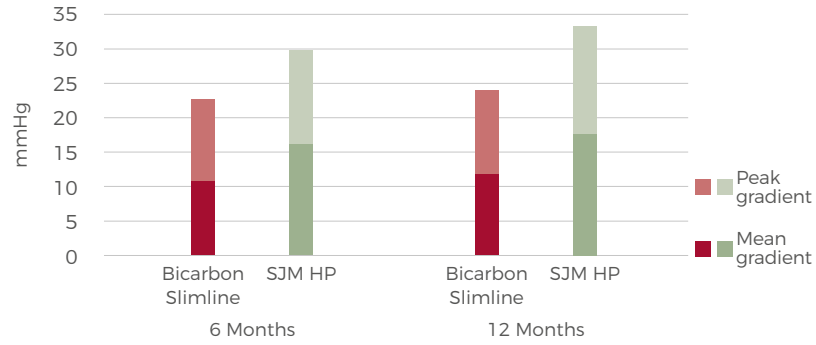


Comparative evaluation of small-size CORCYM Bicarbon Slimline and St. Jude HP heart valve prosthesis.[8]

Size 19 Effective Orifice Area (cm²)



Size 19 Mean and Peak pressure gradients (mmHg)



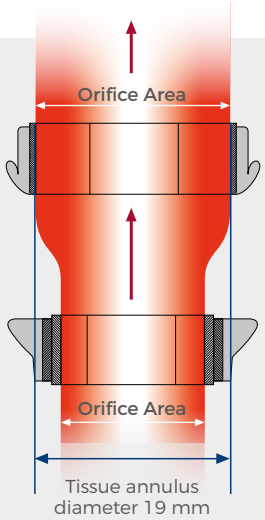
* Bicarbon standard model

Technical claims are supported by CORCYM data on file.

Overline: engineered for hemodynamic performance

To further optimize hemodynamic performances, especially in small aortic annuli, CORCYM features in its Bicarbon portfolio the Overline aortic prosthesis, a truly totally supra-annular model.

A totally supra annular positioning can provide an advantage of 1 to 2 sizes over intra-annular valves.[10]



100% ORIFICE TO ANNULUS MATCH

Overline improves effective valve orifice area thanks to a 100% orifice to annulus match, thus contributing to reduce the risk of PPM.[2,11]

" An 18 mm or 20 mm valve was implanted in more than 80% of the present patients.[...] However, no cases of PPM were observed, despite the use of 18 and 20 mm valves."[2]

Hemodynamic function on echocardiography before and at 12 months after surgery, by labeled valve size.[2]

Parameters	Time	Total pts	Valve size (mm)		
		(n=102)	18 (n=27)	20 (n=51)	22 (n=24)
PPG (mmHg)	Preoperative	67 ± 29	78 ± 24	64 ± 21	62 ± 32
	12 months	24 ± 8	26 ± 8	23 ± 8	24 ± 9
MPG (mmHg)	Preoperative	42 ± 19	50 ± 17	37 ± 19	44 ± 19
	12 months	13 ± 5	15 ± 6	12 ± 4	12 ± 5

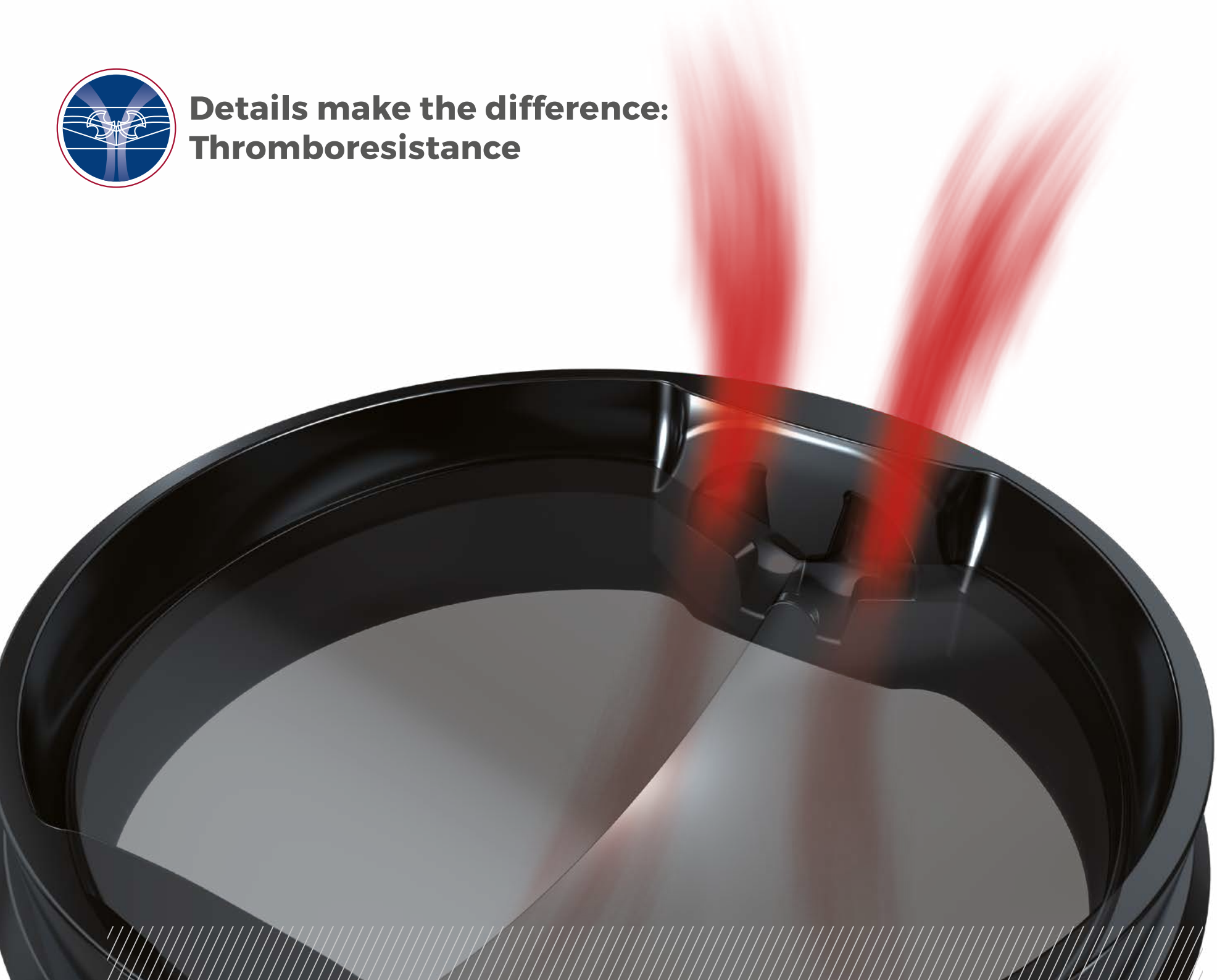
MPG: Mean pressure gradient; PPG: Peak pressure gradient

"The in vivo data showed excellent hemodynamic results for all valve sizes [..]. In addition, the EOA was significantly increased, from 0.80 ± 0.41 cm² before surgery to 2.01 ± 0.26 cm² after 12 months".[2]

1. *Reul et al., In vitro comparison of bileaflet aortic heart valve prostheses, J. Thorac and Cardiov Surg 106 (3): 412-20, 1992.*
2. *Reyes et al., Results of aortic valve replacement with the supra-annular Sorin Bicarbon Overline prosthesis, J Heart Valve Dis, 21 (3): 358-63, 2012.*
3. *Vallana et al., Pivot design in bileaflet valves, Asaio Journal, 38:M600-M606, 1992.*
4. *Della Barbera et al., Sovering annuloplasty rings: Experimental pathology in the sheep model, Cardiovascular Pathology 14 (2005) 96-103.*
5. *Steegers et al., J. Leakage flow at mechanical heart valve prostheses: improved washout or increased blood damage, Heart Valve Dis 8 : 312-323, 1999.*
6. *Bottio et al., Small aortic annulus: The hydrodynamic performances of 5 commercially available bileaflet mechanical valves, J Thorac Cardiovasc Surg 2004;128:457-62.*
7. *Fisher et al., Comparative study of the hydrodynamic function of six size 19 mm bileaflet heart valves, Eur J Cardio-thorac Surg 9: 692-96, 1995.*
8. *Otero et al., Comparative evaluation of small-size Sorin Slimline and St. Jude HP Heart Valve Prostheses., Ann Thorac Surg 79: 1284-90, 2005.*
9. *Badano et al., Normal echocardiographivc characteristics of the Sorin Bicarbon bileaflet prosthetic heart valve in the mitral and aortic positions, J Am Soc Echocardiogr 10: 632- 43, 1997.*
10. *Aagard et al., Maximizing prosthetic valve size with the Top Hat supraannular aortic valve, The Journal of Heart Valve Disease, 16:84-90, 2007.*
11. *Aagard et al., Midterm Evaluation of Hemodynamics of the Top Hat Supraannular Aortic Valve. Asian Cardiovasc Thorac Ann 2010;18:1-5.*

Technical claims are supported by CORCYM data on file.

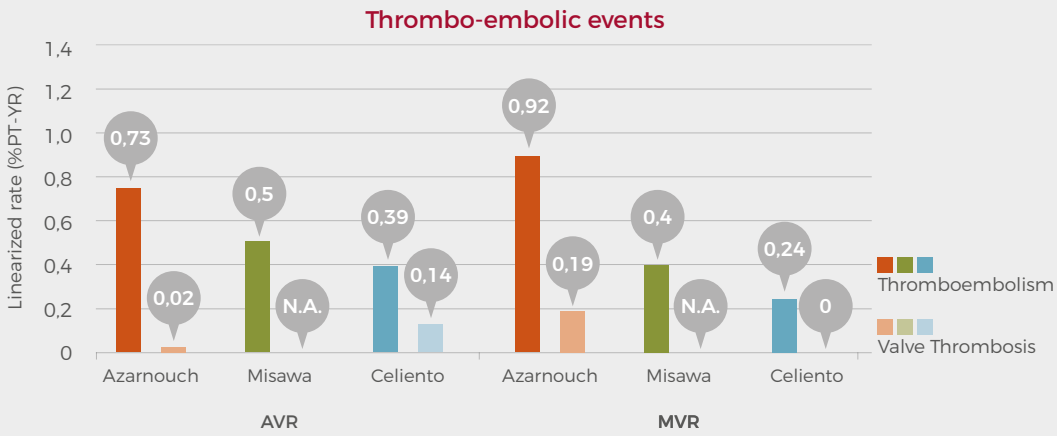
Details make the difference: Thromboresistance



Bicarbon valves are specifically designed to minimize thrombogenicity:[1,2]

- Carbofilm coating increases hemocompatibility lowering the risk of thrombus formation.[3,4*]
- Curved leaflets, aerofoil housing profile, optimized leaflets travel arc and opening angle favor a laminar blood flow which reduces shear stress and hemolysis.[3] A low degree of hemolysis leads to less platelet activation and consequently less risk of clots.[5]
- The unique two-open-chimney design ensures an effective passive washing of the hinges avoiding blood stasis and hemolysis at the same time.[3,6]

Bicarbon valves have shown a very low incidence of thrombosis and thromboembolic events in up to 17 years of published follow up.[7,8,9]



* Based on CORCYM post-market surveillance, valve-related pannus formation is expected to occur between 0.1 and 1 times per 100000 device population.

Technical claims are supported by CORCYM data on file.

LOWERing the INtensity of oral anticoaGulant Therapy in patients with bileaflet mechanical aortic valve replacement: Results from the "LOWERING-IT" Trial.[2]

As a further proof of its excellent thrombo-resistance, Bicarbon is backed by the 'LOWERING-IT' trial, an independent prospective controlled randomized study which has established for the first time that a lower INR target (1.5-2.5) is safe and feasible in low risk patients after aortic valve replacement.[2]

Flow diagram of the LOWERING-IT trial[2]

396 patients included in the analysis

CONVENTIONAL-INR GROUP
PTS assigned to INR 2.0-3.0
199 pts. Included in the Analysis

LOW-INR GROUP
PTS assigned to INR 1.5-2.5
197 pts. Included in the Analysis

3 out of 4 patients in the Low-INR group of the LOWERING-IT Trial had a Bicarbon valve implanted[2]

Outcome events[2]

	LOW-INR (n=197)	CONVENTIONAL-INR (n= 199)	*P*	OR (95% exact CI)
Thromboembolic events	1	3	.62 ns	0.33 (0.006-4.20)
Hemorrhagic events	6	16	.04	0.36 (0.11-0.99)

"LOWERING-IT trial established that the proposed LOW-INR target is safe and feasible in low-risk patients after bileaflet aortic mechanical valve replacement. It results in similar thrombotic events and in a significant reduction of bleeding occurrence when compared to the conventional anticoagulation regimen."[2]

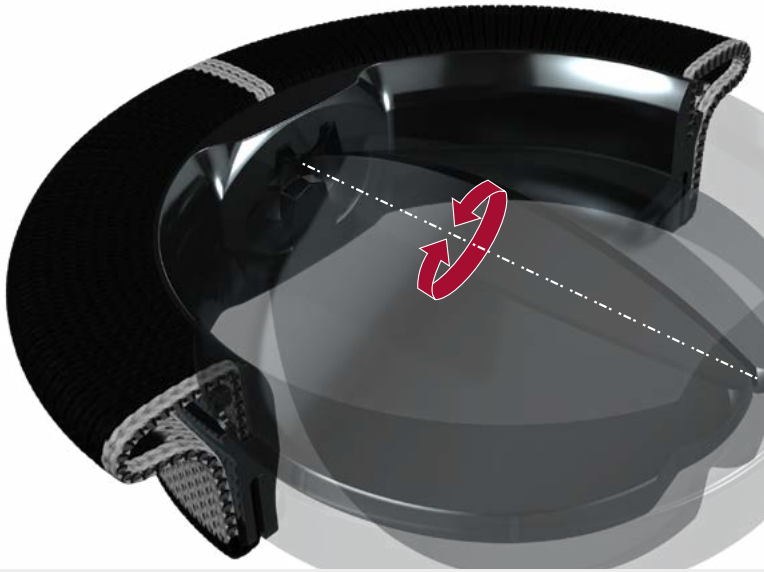
1. Falk et al., European Journal of Cardio-Thoracic Surgery 52 (2017) 616–664.
2. Torella et al., LOWERing the INtensity of oral anticoaGulant Therapy in patients with bileaflet mechanical aortic valve replacement: Results from the "LOWERING-IT" Trial, Am Heart J; 160:171-8, 2010.
3. Vallana et al., Pivot design in bileaflet valves, Asaio Journal, 38:M600-M606, 1992.
4. Della Barbera et al., Sovering annuloplasty rings: Experimental pathology in the sheep model, Cardiovascular Pathology 14 (2005) 96-103.
5. Koppensteiner et al., Blood rheology after cardiac valve replacement with mechanical prostheses or bioprostheses, Am J Cardiolo; 67:79-83, 1991.
6. Steegers et al., J. Leakage flow at mechanical heart valve prostheses: improved washout or increased blood damage, Heart Valve Dis 8 : 312-323, 1999.
7. Azarnoush et al., The Sorin Bicarbon over 15 years clinical outcomes: multicentre experience in 1704 patients, Eur J Cardio-thoracic Surg; 38:759—66, 2010.
8. Misawa et al., Fifteen-year experience with the Bicarbon heart valve prosthesis in a single center, J Cardiothorac Surg, 10: 89, 2015.
9. Celiento et al., Single center experience with the Sorin Bicarbon prosthesis: A 17-year clinical follow-up, J Thorac Cardiovasc Surg, 148:2039-44, 2014.

Technical claims are supported by CORCYM data on file.

Details make the difference: Safety and Durability

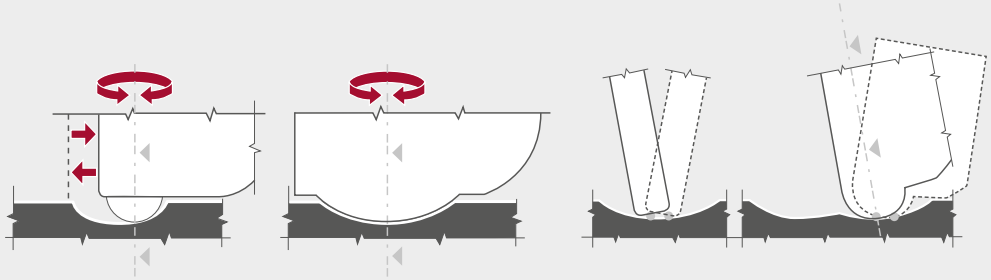
The Bicarbon design was carefully engineered to last over time.*

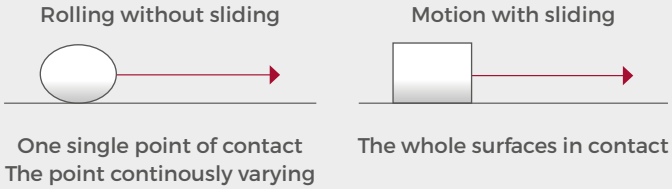
- The Titanium housing, with greater structural stability than solid Pyrolytic Carbon housings, ensures correct leaflet functionality.[1]
- The unique two-open-chimney design of the hinges avoid blood stasis and hemolysis minimizing the risk of structural valve failure and clinical complications.[1,2]
- The Carbofilm coated PET fabric sewing ring provides a safe anchorage favoring a gentle tissue ingrowth that minimizes pannus formation.**
- The unique, proprietary 'rolling without sliding' hinge mechanism, characterized by a constantly varying single point of contact between the pivot and the housing, minimizes friction and wear and consequently the risk of structural valve deterioration.[1,2]



The innovative Bicarbon solution

Friction and wear are minimized by the constantly varying single point of contact between the pivot and the housing.[1,2]





* According to ISO 5840:2015 requirements, CORCYM post-market surveillance and published experience on long term results (Celiento et al., J Thorac Cardiovasc Surg, 148:2039-44, 2014).
** Based on CORCYM post-market surveillance, valve-related pannus formation is expected to occur between 0.1 and 1 times per 100000 device population.

1. Vallana et al., Pivot design in bileaflet valves, Asaio Journal, 38:M600-M606, 1992.
2. Steegers et al., J. Leakage flow at mechanical heart valve prostheses: improved washout or increased blood damage, Heart Valve Dis 8 : 312-323, 1999.

Technical claims are supported by CORCYM data on file.

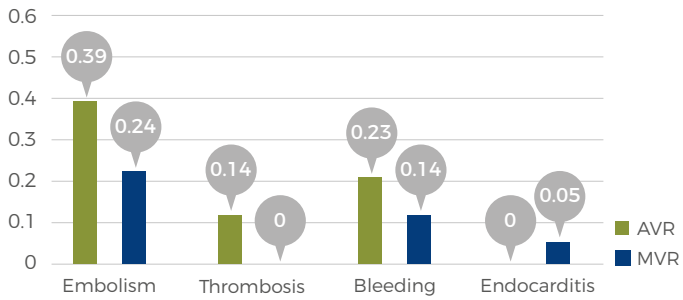
Details make the difference: Clinical outcomes

Bicarbon has proven to be a safe, high performing valve with desirable clinical outcomes in the long term follow up.[1,2]

Single center experience with the CORCYM Bicarbon prosthesis: A 17-year clinical follow-up

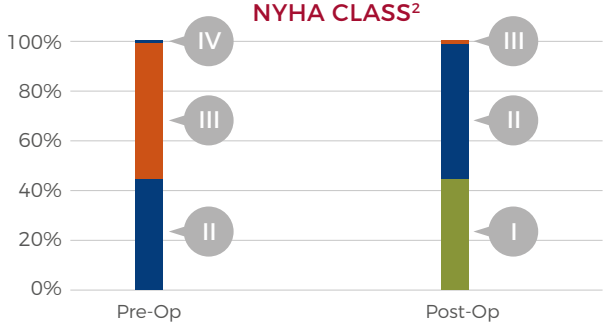
AVR: 344 Patients - MVR: 163 Patients - Cumulative follow-up: 6475 Patient-years

Linearized rate of adverse events (%PT-YR)[2]



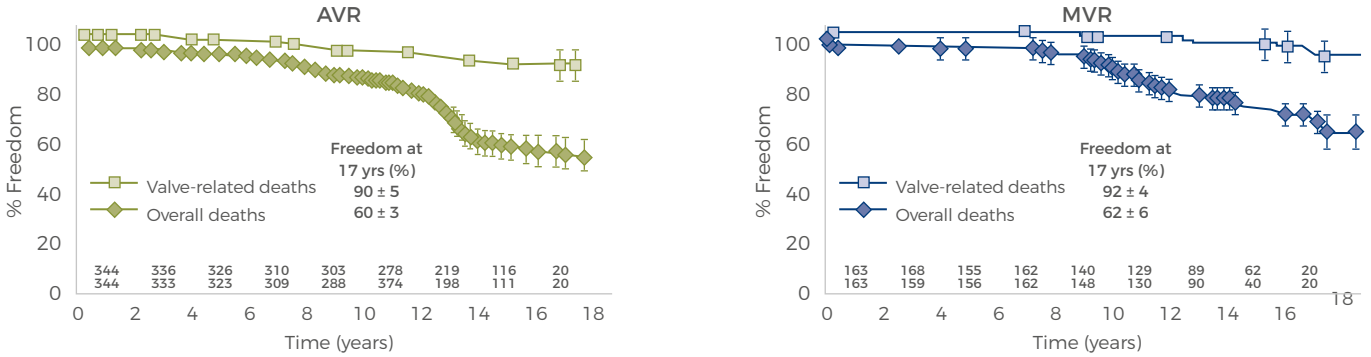
Mean INR at last FU: AVR: 2.6±0.5 - MVR: 2.7±0.4

NYHA CLASS[2]



"The Bicarbon Prosthesis has shown excellent results in terms of clinical improvement and freedom from valve-related complications, even up to 17 years after AVR and MVR." [2]

Actuarial Survival and Freedom from valve-related deaths[2]



Numbers on the horizontal axis indicate patients at risk at each time interval

1. Azarnoush et al., The Sorin Bicarbon over 15 years clinical outcomes: multicentre experience in 1704 patients, Eur J Cardio-thoracic Surg; 38:759—66, 2010.
2. Celiento et al., Single center experience with the Sorin Bicarbon prosthesis: A 17-year clinical follow-up, J Thorac Cardiovasc Surg, 148:2039-44, 2014.

BICARBON FAMILY

The voice of experience

"The Bicarbon Prosthesis continues to perform satisfactorily even in the long term with low incidence of valve-related mortality and morbidity confirming to be an extremely reliable and durable mechanical valve substitute."[1]*

"In the present series, a low incidence of embolic events was observed [...] indicating that the innovative changes incorporated into the Bicarbon Prosthesis design, improving transprosthetic flow and reducing turbulence, might positively influence its thrombogenicity."
"We have also found that other major postoperative complications, [...] are extremely uncommon after AVR and MVR with the Bicarbon Prosthesis."
"[...] no cases of structural failure were recorded."[2]*

"The present study gives additional evidence of low rates of valve-related complications after Bicarbon valve Implantation. [...] we maintain the INR between 1.8 and 3.0. The rate of thromboembolic events in this study is excellent and the rates of bleeding complications are also acceptable."
"This single-center study of a 15-year follow-up of the Bicarbon prosthetic heart valve shows excellent clinical results associated with a low incidence of valve-related mortality and morbidity."[3]*

* CORCYM post-market surveillance classifies the incidence of valve structural failure *P* as very improbable ($P \leq 10\text{-}6$) and the incidence of valve related thromboembolic events *P*1 as improbable ($10\text{-}6 < P1 \leq 10\text{-}5$).

1. *Azarnoush et al., The Sorin Bicarbon over 15 years clinical outcomes: multicentre experience in 1704 patients, Eur J Cardio-thoracic Surg; 38:759-66, 2010.*
2. *Celiento et al., Single center experience with the Sorin Bicarbon prosthesis: A 17-year clinical follow-up, J Thorac Cardiovasc Surg, 148:2039-44, 2014.*
3. *Misawa et al., Fifteen-year experience with the Bicarbon heart valve prosthesis in a single center, J Cardiothorac Surg, 10: 89, 2015.*

Technical claims are supported by CORCYM data on file.

BICARBON™ FAMILY MECHANICAL HEART VALVES

BICARBON OVERLINE

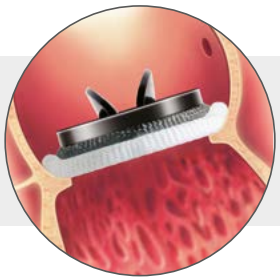
Implantation Consideration

- Totally supra-annular placement
  - provides an advantage of 1 to 2 sizes over intra-annular valves[1]
  - facilitates double valve replacement procedure[2]
- Orientation of the implanted valve facilitated by a Polyacetal sleeve mounted inside the sewing cuff, which maintains torque at a constant level
- Three orientation markers for suture spacing
- Soft, pliable cuff for easy handling and better conformity to the patient's annulus
- Special sizers allow surgeon to assess position of valve within sinus area and clearance of coronaries before implantation

Clinical Consideration

- Advanced design optimized for favorable hemodynamic performance[2,5]
- Special sizers allow surgeon to assess position of valve within sinus area and clearance of coronaries before implantation
- Size upgrades provide improved valve hemodynamics[1]*
- Totally supra-annular design allows a 100% orifice to annulus match, maximazing the orifice available to blood flow
- Alternative to aortic root enlargement[2]
- Advanced design allows to achieve a laminar blood flow that minimizes the risk of thrombus formation[4]
- Very low valve-related adverse events[2,5,6]**
- Proven safety and durability[2,5]***

Valve Placement *in-situ*



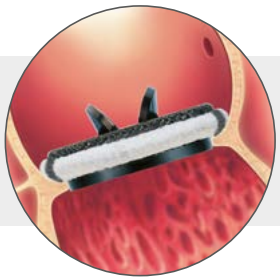
BICARBON SLIMLINE

Implantation Consideration

- A partially supra-annular solution when in need of larger orifice areas compared to intra-annular valves[3]
- Orientation of the implanted valve facilitated by a Polyacetal sleeve mounted inside the sewing cuff, which maintains torque at a constant level
- Three orientation markers for suture spacing
- Soft, pliable cuff for easy handling and better conformity to the patient's annulus

Clinical Consideration

- Special sizers allow surgeon to assess position of valve within sinus area and clearance of coronaries before implantation
- Advanced design allows to achieve a laminar blood flow that minimizes the risk of thrombus formation[4]
- Very low valve-related adverse events[2,5]**
- Proven safety and durability[2,5]***



*Compared to non totally supra-annular models.

**Based on CORCYM post-market surveillance, valve structural failure is expected to occur less than 1 time per 1000000 device population, while valve-related thromboembolic events are expected to occur between 0.1 and 1 times per 100000 device population.

***Based on CORCYM post-market surveillance, valve structural failure is expected to occur less than 1 time per 1000000 device population.

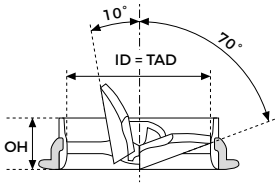
Technical claims are supported by CORCYM data on file.

1. *Aagard et al., Maximizing prosthetic valve size with the Top Hat supraannular aortic valve, The Journal of Heart Valve Disease, 16:84-90, 2007.*
2. *Reyes et al., Results of aortic valve replacement with the supra-annular Sorin Bicarbon Overline prosthesis, J Heart Valve Dis, 21 (3): 358-63, 2012.*
3. *Otero et al., Comparative evaluation of small-size Sorin Slimline and St. Jude HP Heart Valve Prostheses, Ann Thorac Surg 79: 1284-90, 2005.*
4. *Vallana et al., Pivot design in bileaflet valves, Asaio Journal, 38:M600-M606, 1992.*
5. *Badano et al., Normal echocardiographivc characteristics of the Sorin Bicarbon bileaflet prosthetic heart valve in the mitral and aortic positions, J Am Soc Echocardiogr 10: 632- 43, 1997.*
6. *Celiento et al., Single center experience with the Sorin Bicarbon prosthesis: A 17-year clinical follow-up, J Thorac Cardiovasc Surg, 148:2039-44, 2014.*

BICARBON OVERLINE

TOTALLY SUPRA-ANNULAR AORTIC VALVE Sizes 16-24 mm

Product specifications



Nominal size	TAD	ID	OH	GOA	EOA[1]	Catalog N.
16	15.2	15.2	6.0	1.76	0.97	ICV0870
18	17.2	17.2	6.4	2.27	1.54	ICV0871
20	19.2	19.2	6.8	2.83	2.07	ICV0872
22	21.3	21.3	7.2	3.45	2.39	ICV0873
24	23.3	23.3	7.6	4.14	3.06	ICV0874

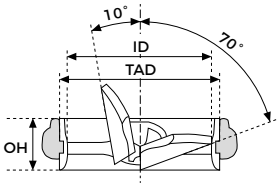
Accessories

Article	Code	Description
UNI cylindrical sizers set	ICV0867	5 sizers
Aortic rotators set	ICV0868	5 aortic rotators
UNI handle	ICV0664	1 universal bandable handle to be used with all sizers
Valve holder handle	P0593	1 Nitinol bandable handle
Occluder tester	VT-100	10 disposable occluder tester (provided sterile)
Empty tray	TR-101	1 empty tray

BICARBON SLIMLINE

PARTIALLY SUPRA-ANNULAR AORTIC VALVE Sizes 17-27 mm

Product specifications



Nominal size	TAD	ID	OH	GOA	EOA[1]	Catalog N.
17	17.2	15.2	6.0	1.76	1.01[2]	ICV0934
19	19.2	17.2	6.4	2.27	1.50[2]	ICV0935
21	21.3	19.2	6.8	2.83	1.90[2]	ICV0936
23	23.4	21.3	7.2	3.45	2.39[1]	ICV0937
25	25.6	23.3	7.6	4.14	3.06[1]	ICV0938
27	28.0	25.6	8.0	5.0	3.45[1]	ICV0939

Accessories

Article	Code	Description
UNI cylindrical sizers set	ICV0728	6 universal cylindrical sizers
UNI profile sizers set	ICV0730	6 universal profile sizers
Aortic rotators set	ICV0950	6 aortic rotators
UNI handle	ICV0664	1 universal bandable handle to be used with all sizers
Valve holder handle	P0593	1 Nitinol bandable handle
Occluder tester	VT-100	10 disposable occluder tester (provided sterile)
Empty tray	TR-101	1 empty tray

Legend

TAD = Tissue Annulus Diameter (mm)	EOA = In vivo Effective Orifice Area (cm²)	GOA = Geometric Orifice Area (cm²)
ID = Internal Diameter (mm)	OH = Orifice Height (mm)	

1. *Badano et al., Normal echocardiographivc characteristics of the Sorin Bicarbon bileaflet prosthetic heart valve in the mitral and aortic positions, J Am Soc Echocardiogr 1997; 10: 632- 43.*
2. *Otero et al., Comparative evaluation of small-size Sorin Slimline and St. Jude HP Heart Valve Prostheses, Ann Thorac Surg 2005; 79: 1284-90.*

BICARBON FITLINE AORTIC

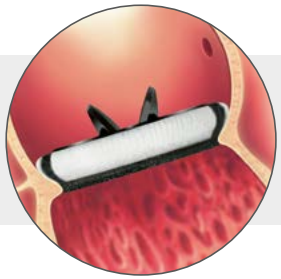
Implantation Consideration

- Orientation of the implanted valve facilitated by a Polyacetal sleeve mounted inside the sewing cuff, which maintains torque at a constant level
- Three orientation markers for suture spacing
- Soft, pliable cuff for easy handling and better conformity to the patient's annulus

Clinical Consideration

- Special sizers allow surgeon to assess position of valve within sinus area and clearance of coronaries before implantation
- Advanced design allows to achieve a laminar blood flow that minimizes the risk of thrombus formation[1]
- Very low valve-related adverse events*
- Proven safety and durability**

Valve Placement *in-situ*



BICARBON FITLINE MITRAL

Implantation Consideration

- Orientation of the implanted valve facilitated by a Polyacetal sleeve mounted inside the sewing cuff, which maintains torque at a constant level
- Four orientation markers for suture spacing
- Soft, pliable cuff for an easy handling and to better conform to the patient's annulus, promotes coaptation to annulus

Clinical Consideration

- Special sizers allow surgeon to assess position of valve within sinus area and clearance of coronaries before implantation
- Advanced design allows to achieve a laminar blood flow that minimizes the risk of thrombus formation[1]
- Very low valve-related adverse events*
- Proven safety and durability**

Valve Placement *in-situ*

*CORCYM post-market surveillance classifies the incidence of valve structural failure *P* as very improbable ($P \leq 10\text{-}6$) and the incidence of valve-related thromboembolic events *P*1 as improbable ($10\text{-}6 < P1 \leq 10\text{-}5$).

**CORCYM post-market surveillance classifies the incidence of valve structural failure *P* as very improbable ($P \leq 10\text{-}6$).

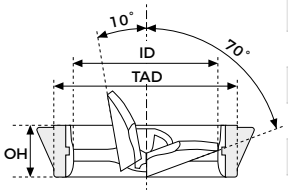
1. *Vallana et al., Pivot design in bileaflet valves, Asaio Journal, 38:M600-M606, 1992.*

Technical claims are supported by CORCYM data on file.

BICARBON FITLINE AORTIC

INTRA-ANNULAR AORTIC VALVE Sizes 19-31 mm

Product specifications

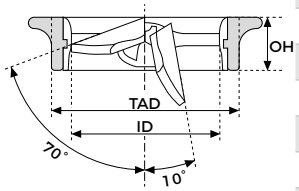


Nominal size	TAD	ID	OH	GOA	EOA[1]	Catalog N.
19	19.0	15.2	6.0	1.76	0.97	ICV0917
21	21.2	17.2	6.4	2.27	1.54	ICV0918
23	23.4	19.2	6.8	2.83	2.07	ICV0919
25	25.6	21.3	7.2	3.45	2.39	ICV0920
27	27.8	23.3	7.6	4.14	3.06	ICV0921
29	30.0	25.6	8.0	5.00	3.45	ICV0922
31	32.0	25.6	8.0	5.00	3.45	ICV0923

BICARBON FITLINE MITRAL

Sizes 19-33 mm

Product specifications



Nominal size	TAD	ID	OH	GOA	Catalog N.
19	19.0	15.2	6.0	1.76	ICV0924
21	21.2	17.2	6.4	2.27	ICV0925
23	23.4	19.2	6.8	2.83	ICV0926
25	25.6	21.3	7.2	3.45	ICV0927
27	27.8	23.3	7.6	4.14	ICV0928
29	30.0	25.6	8.0	5.00	ICV0929
31	32.0	25.6	8.0	5.00	ICV0930
33	34.0	25.6	8.0	5.00	ICV0931

Accessories

Article	Code	Description
UNI cylindrical sizers set	ICV0662	8 universal cylindrical sizers
UNI profile sizers set	ICV0663	8 universal profile sizers
Rotators set	ICV0732	6 aortic rotators + 6 mitral rotators
UNI handle	ICV0664	1 universal bandable handle to be used with all sizers and mitral rotators
Valve holder handle	P0593	1 Nitinol bandable handle
Occluder tester	VT-100	10 disposable occluder tester (provided sterile)
Empty tray	TR-101	1 empty tray

Legend

TAD = Tissue Annulus Diameter (mm)	EOA = In vivo Effective Orifice Area (cm²)	GOA = Geometric Orifice Area (cm²)
ID = Internal Diameter (mm)	OH = Orifice Height (mm)	

1. *Badano et al., Normal echocardiographivc characteristics of the Sorin Bicarbon bileaflet prosthetic heart valve in the mitral and aortic positions, J Am Soc Echocardiogr 1997; 10: 632- 43.*

INTENDED USE/INDICATIONS

The Bicarbon prosthesis is intended for use as a replacement valve in patients with diseased, damaged, or malfunctioning mitral or aortic heart valve. This device may also be used to replace a previously implanted mitral or aortic prosthetic heart valve.
Bicarbon Aortic/Mitral prostheses, respectively, are indicated for use in patients suffering from aortic/mitral valvular heart disease, that is a condition involving obstruction of the aortic/mitral heart valve or stenosis; leakage of the aortic/mitral valve, known as regurgitation, incompetence, or insufficiency; and combinations of the two; or patients with a previously implanted aortic/mitral valve prosthesis that is no longer functioning adequately and requires replacement.

KEY CONTRAINDICATIONS

The Bicarbon prostheses are contraindicated in patients at risk for complications associated with long-term anticoagulant treatment that clinical experience has shown to be indispensable for patients with mechanical heart valves.

KEY WARNINGS

For single use only. The use of the Bicarbon prostheses is not recommended in patients with hypersensitivity to Titanium alloys and to Cobalt Chromium alloys (Stellite). Do not manipulate the Bicarbon prosthesis with instruments other than those supplied by Corcym srl.

TOP POTENTIAL SIDE EFFECTS

The complications associated with heart valve prosthesis implantation include: hemolysis, infections, thrombosis or thromboembolic events, dehiscence, unacceptable hemodynamic performance, hemorrhagic events due to anticoagulant therapy, prosthesis malfunction, heart failure, myocardial infarction due to coronary obstruction, allergic reaction and death. Any one of these complications may require re-operation or removal of the prosthesis.

MRI conditional

For professional use. Please contact us through our website to receive instructions for use containing full prescribing information, including indications, contraindications, warnings, precautions and adverse events. Not approved in all geographies. Consult your labeling.

CORCYM
WE TAKE LIFE TO HEART

Manufactured by:

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Via per Crescentino sn
13040 Saluggia (VC) Italy
Tel: +39 0161 487800

CE 0123

corcym
.com

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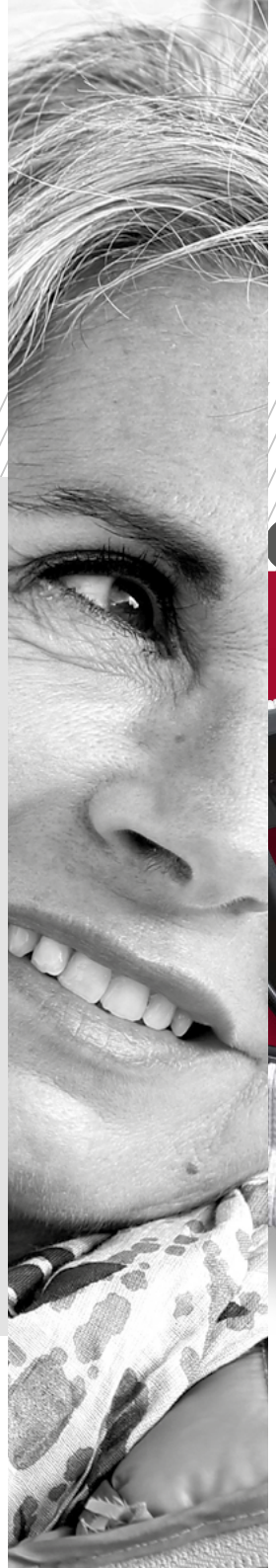


MECHANICAL
HEART VALVES

CARBOMEDICS™ FAMILY

Tailored reliability
for Patients and
Surgeon

CORCYM
WE TAKE LIFE TO HEART

CARBOMEDICS™ FAMILY

Bileaflet mechanical heart valves

With its Carbomedics™ line of products CORCYM offers cardiac Surgeons and Patients a complete set of mechanical heart valve solutions to reliably treat even the challenging cases.[2]

The Carbomedics name is intrinsically linked to the historical development of mechanical heart valves.

Based on the expertise and with the clear mission of providing highly reliable and technologically advanced solutions, in 1986 Carbomedics introduced to the market a mechanical bileaflet valve with a rotatable housing for optimal leaflet positioning.

Since this first step, the Carbomedics portfolio has been enriched over time up to the current, complete set of solutions that offer Surgeons flexibility while treating their Patients.

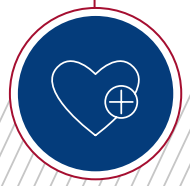
Choosing a Carbomedics mechanical valve today means choosing a reliable solution with proven clinical results in over 20 years of follow up and an extremely low incidence of post-operative structural failures reported in over 1 million implants.*[1]

* CORCYM post-market surveillance classifies the risk of structural valve failure *P* as improbable ($10^{-6} < P \leq 10^{-5}$).

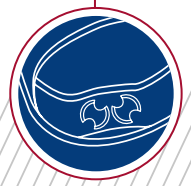
1. *Bouchard et al., Twenty-Year Experience With the CarboMedics Mechanical Valve Prosthesis. Ann Thorac Surg 2014;97:816–23.*
2. *Nishida et al., Single-institution, 22-year follow-up of 786 CarboMedics mechanical valves used for both primary surgery and reoperation. J Thorac Cardiovasc Surg 2014;147:1493-8).*

Tailored options for desirable Patient outcomes[1]

Tailored safety and durability[1]

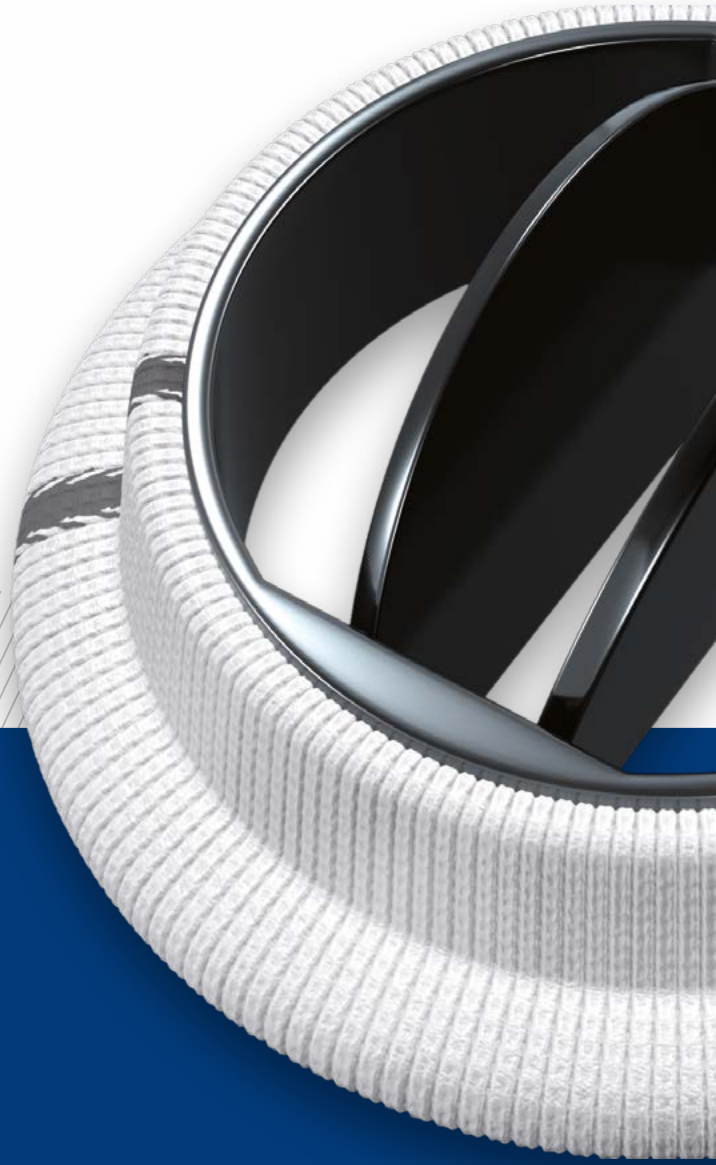


Tailored performance for desirable clinical outcomes



Tailored ease of implant

Tailored solutions for Patients and Surgeons



1. Bouchard et al., Twenty-Year Experience With the CarboMedics Mechanical Valve Prosthesis. Ann Thorac Surg 2014;97:816–23.

Tailored safety and durability[1]

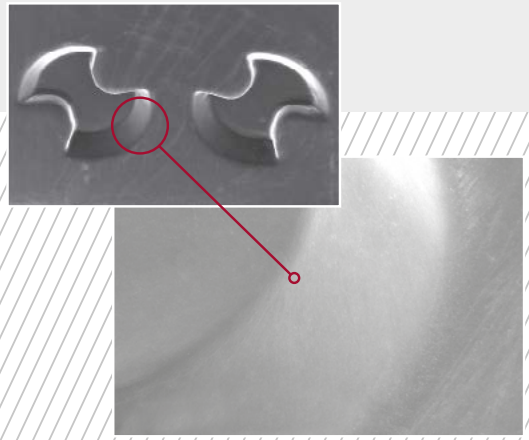
Historically focused on biocompatible materials

Thanks to its robust design, the Carbomedics bileaflet mechanical heart valve has extremely low incidence of post-operative structural failures in over 1 million implants worldwide.*

Carbomedics Pyrolite® Carbon is engineered to provide excellent thromboresistance* and mechanical resistance.[1]

This is achieved by co-depositing a small amount of Silicon during the manufacturing process, because the Silicon acts as a reinforcing element to the crystal structure of Pyrolytic Carbon.[1] The surface is then polished to remove the superficial roughness, thus achieving a mirror like finish.[1,2]

Polished Silicon alloyed varieties of Pyrolytic Carbon exhibit an excellent degree of thromboresistance while improving resistance to wear, offering results proven by over 20 years of clinical follow up.[1,2]



* CORCYM post-market surveillance classifies the risk of structural valve failure *P* as improbable (10-6 < *P* ≤ 10-5).

1. *J.C. Bokros Carbon Biomedical Devices. - Carbon, 1977;15:355-71.*
2. *Goodman et al., Platelet responses to silicon-alloyed pyrolytic carbons. - Wiley Periodicals, Inc. J Biomed Mater Res 83A: 64–69, 2007*

Technical claims are supported by CORCYM data on file.

A robust design* to minimize post-operative structural failures

Pyrolytic carbon coated leaflets

The leaflets of the Carbomedics valves are made of a substrate of tungsten filled graphite coated with Pyrolite® Carbon. The presence of Tungsten provides better radiopacity allowing a non invasive diagnostic observation of the leaflets' motion through fluoroscopy or similar methodologies.

The CORCYM proprietary Carbofilm coating is applied to both the valve's Titanium housing and the sewing cuff. The coating favors hemocompatibility, minimizing the risk for pannus formation* and favoring a gentle tissue ingrowth.[3,4]

Pyrolytic carbon housing

Differently from other substrate processes, which results in a graphite core coated with pyrolytic carbon, Carbomedics valves employ an advanced mandrel process resulting in a low profile housing made entirely of Pyrolite® Carbon.

The mandrel process allows pivots to be located within the housing, reducing pannus ingrowth and interference with leaflet motion that can occur around the protruding “pivot ear” design.[1,2] Moreover, it permits a more sophisticated design of the pivot, the shape of which grants total washing of its entire surface, minimizing thromboembolic events**.[3]

Structural components

To further enhance structural stability, the housing is reinforced by a titanium stiffening band which makes it stronger than a valve without a stiffening element, minimizing the risk of deformation and, consequently, the risk of leaflet dislodgement or lockup.[3,4]
A lock wire forms a solid mechanical bond between the housing and the titanium reinforcement band while creating a track for rotation.

Secure attachment of the sewing cuff to the housing is ensured by double lock wires.

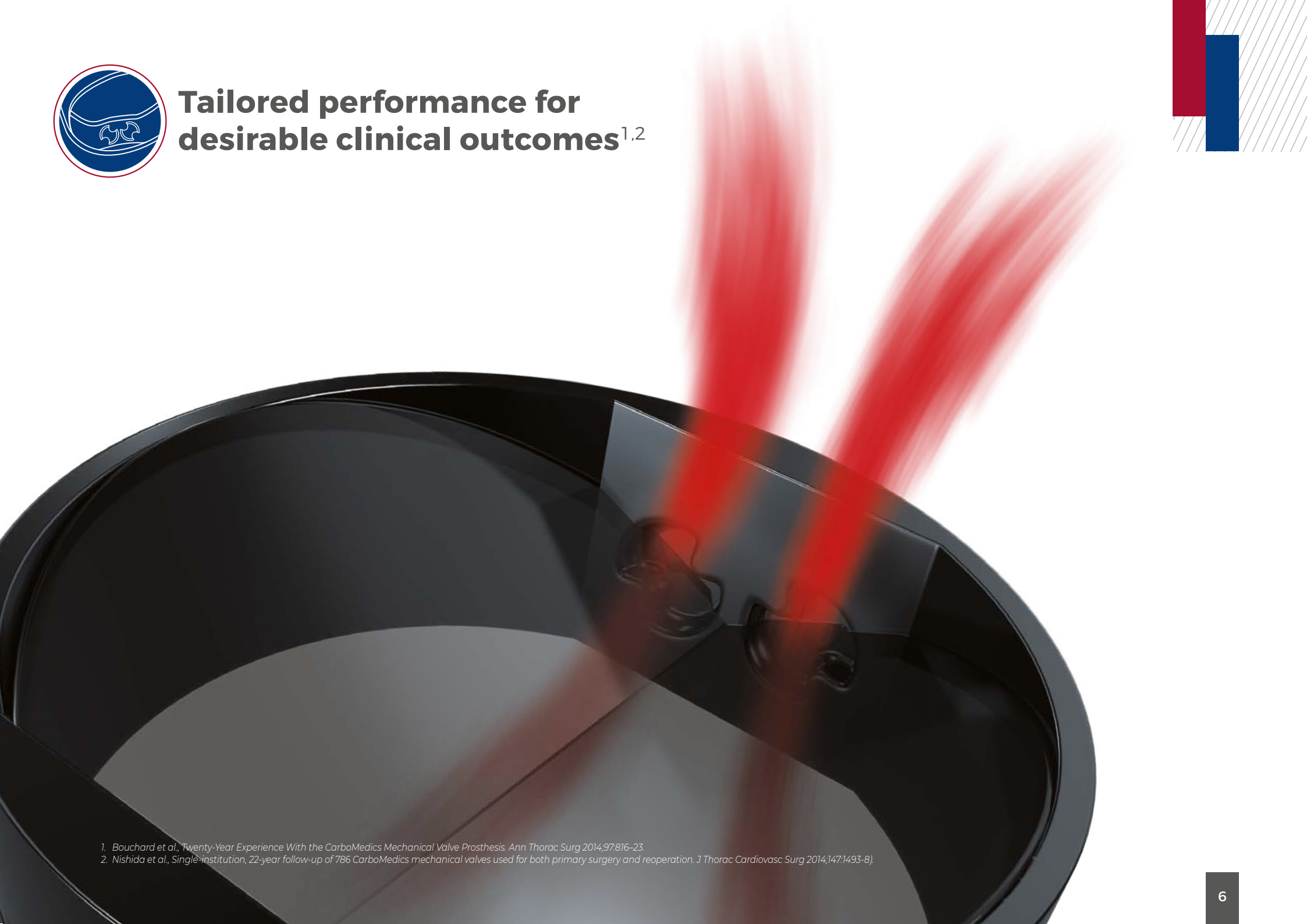
* According to ISO 5840:2015 requirements, CORCYM post-market surveillance and published experience on long term results (Bouchard et al., Ann Thorac Surg 2014;97:816-23).

** Falk et al., European Journal of Cardio-Thoracic Surgery 52 (2017) 616-664.

1. *Aoyagi et al., Obstruction of St Jude medical valves in the aortic position: a consideration for pathogenic mechanism of prosthetic valve obstruction. - Cardiovasc Surg. 2002 Aug;10(4):339-44.*
2. *Dearani et Al., Entrapment of subvalvular mitral tissue causing intermittent failure of a St Jude mitral prosthesis. - J Am Soc Echocardiogr. 2000 Dec;13(12):1121-3.*
3. *Chambers et al., Echocardiographic Description Of The Carbomedics Bileaflet Prosthetic Heart Valve. - J Am Coll Cadiol 1993;21:398-405.*
4. *Bernal et al., The CarboMedics Valve: Experience With 1,049 Implants. - Ann Thorac Surg 1999;67:1299-303*

Technical claims are supported by CORCYM data on file.

Tailored performance for desirable clinical outcomes[1,2]



1. Bouchard et al., Twenty-Year Experience With the CarboMedics Mechanical Valve Prosthesis. Ann Thorac Surg 2014;97:816–23.
2. Nishida et al., Single-institution, 22-year follow-up of 786 CarboMedics mechanical valves used for both primary surgery and reoperation. J Thorac Cardiovasc Surg 2014;147:1493-8).

Carbomedics valves are engineered to achieve proven clinical benefits for Patients throughout their lifetime[1,2]

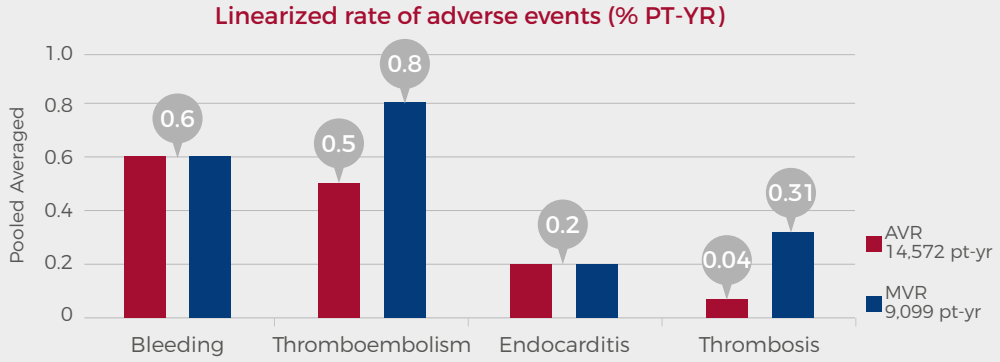
In its long clinical history, Carbomedics valves have demonstrated great levels of safety and reliability, with a considerably low incidence of complications and post-operative structural failures.[1,3]

The enhanced orifice hinge design allows for low thrombogenicity, minimizing pannus overgrowth. The inner surfaces of the pivots are completely open to the flow for washing when the leaflets are closed.[4]

The effectiveness of the Carbomedics design is reflected in the very low linearized rates* (%/pt-yr) of thromboembolic events reported in published scientific literature.

Twenty-Year Experience With the CarboMedics Mechanical Valve Prosthesis[1]

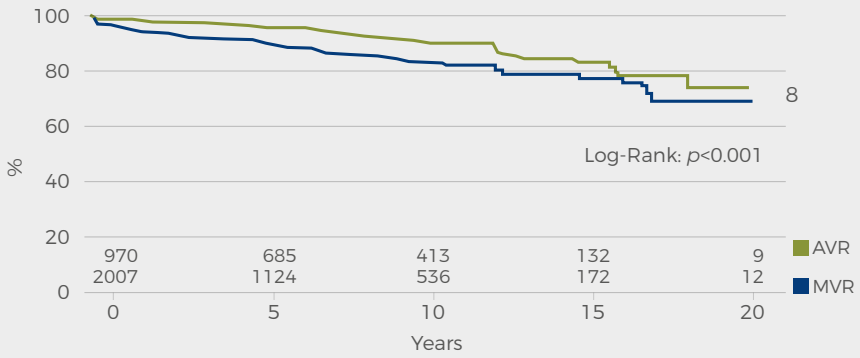
Over **twenty years** of published follow up reports "excellent functional results".[1]



* Objective performance criteria (OPC) as defined in ISO 5840:2012 used for comparison.
CORCYM post-market surveillance classifies the risk of thromboembolic events *P* as improbable (10-6 < *P* ≤ 10-5)[1,3,5]

1. *Bouchard et al., Twenty-Year Experience With the CarboMedics Mechanical Valve Prosthesis. - Ann Thorac Surg 2014;97:816–23.*
2. *CER-00001*
3. *Aagard. Fifteen Years' Clinical Experience with the CarboMedics Prosthetic Heart Valve. - J Heart V Dis 2005 Jan;14(1): 82-8.*
4. *Chambers et al., Echocardiodgraphic Description Of The Carbomedics Bileaflet Prosthetic Heart Valve. - J Am Coll Cadiol 1993;21:398-405.*
5. *Nishida et al., Single-institution, 22-year follow-up of 786 CarboMedics mechanical valves used for both primary surgery and reoperation. J Thorac Cardiovasc Surg 2014;147:1493-8).*

Freedom from valve-related mortality after mitral and aortic valve replacement*.[1,2]



Proven reliability with very low thrombogenicity[3].

Thrombogenicity remains to date one of the major concerns related to the implantation of mechanical heart valves. The safety of the Carbomedics valve with respect to thrombogenicity has been extensively proved in published scientific literature** and is well recognized by the current European guidelines for heart valve disease management which classify Carbomedics as a Low thrombogenic prosthesis.[3]

* All sudden or unknown causes of death were considered valve related in accordance to the Guidelines for reporting morbidity and mortality after cardiac valvular operations.

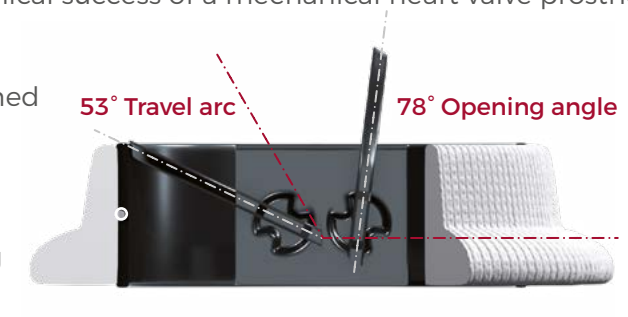
** CORCYM post-market surveillance classifies the risk of structural valve failure *P* as improbable ($10\text{-}6 < P \leq 10\text{-}5$).

1. *Bouchard et al., Twenty-Year Experience With the CarboMedics Mechanical Valve Prosthesis. - Ann Thorac Surg 2014;97:816–23.*
2. *Edmunds et al., Guidelines for reporting morbidity and mortality after cardiac valvular operations. - J Thorac Cardiovasc Surg 1996;112:708–11.*
3. *Falk et al., 2017 ESC/EACTS Guidelines for the management of valvular heart disease. The Task Force for the Management of Valvular Heart Disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS) - European Journal of Cardio-Thoracic Surgery 52 (2017) 616–664*

A unique platform with favorable hemodynamics.[1,2]

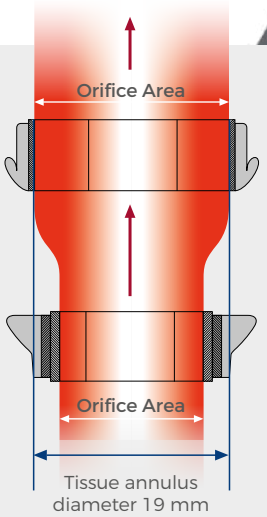
One of the key factors influencing the clinical success of a mechanical heart valve prosthesis is its hemodynamic efficiency.

The opening angle and travel arc of the Carbomedics valves' leaflets are determined by hydrodynamic testing in order to achieve low pressure gradients and an optimal balance between forward flow and regurgitant volume, thus minimizing total energy loss while promoting quiet functioning.



Top Hat, top hemodynamic performance.[1,3]

To further optimize hemodynamics, especially in small aortic annuli, CORCYM features in its Carbomedics portfolio the Top Hat prosthesis, a truly totally supra-annular model which provides an advantage of 1 to 2 sizes over intra-annular valves.[3,4,5] Top Hat improves effective valve orifice area thanks to a 100% orifice to annulus match, thus contributing to reduce the risk of PPM.[1]



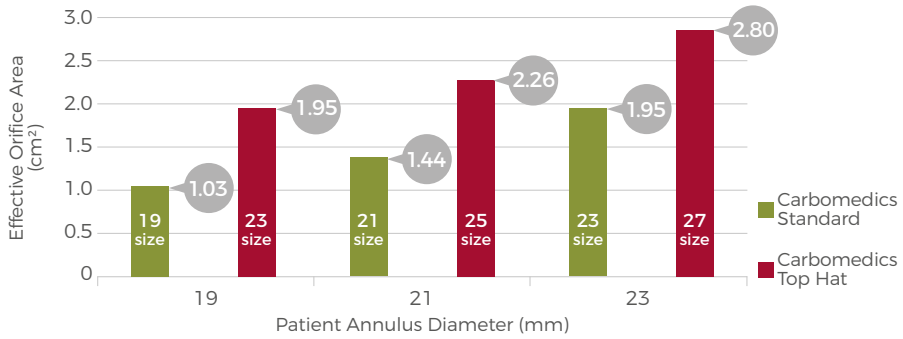
100% ORIFICE TO ANNULUS MATCH

"The Top Hat valve minimizes the risk of patient-prosthesis mismatch, improves hemodynamic performance, and thereby reduces morbidity and mortality".[5]

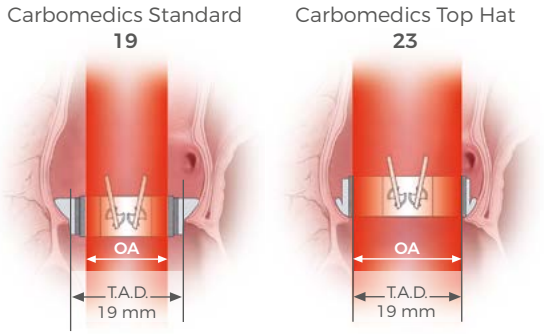
1. *Aagard et al., Midterm Evaluation of Hemodynamics of the Top Hat Supraannular Aortic Valve. - Asian Cardiovasc Thorac Ann 2010;18:1–5.*
2. *Bernal et al., The CarboMedics Valve: Experience With 1,049 Implants. - Ann Thorac Surg 1999;67:1299-303.*
3. *Lundblad R et al., The Carbomedics Supraannular Top hat Valve improves prosthesis size in the Aortic Root. - J Heart Valve Dis 2001;10:196-201.*
4. *Supra annular model as defined by International Standard for Cardiovascular implants - Cardiac valve Prostheses-Part 2. ISO 5840-2:2015(E).*
5. *Aagard et al., Maximizing prosthetic valve size with the Top Hat supraannular aortic valve.- The Journal of Heart Valve Disease 2007;16:84-90.*

Technical claims are supported by CORCYM data on file.

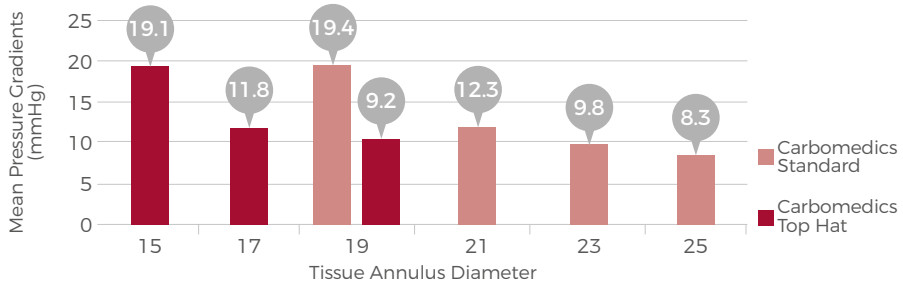
Carbomedics *in vitro* data*

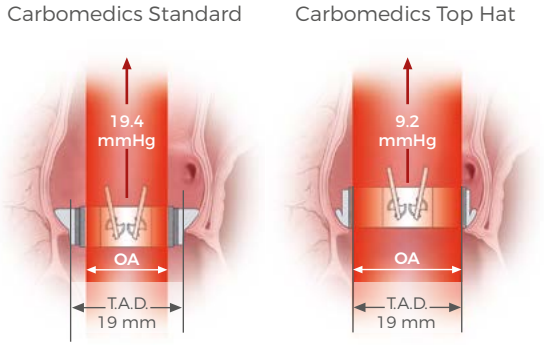


**In vitro test - 5l/min 70 bpm (Data on file at CORCYM)



Carbomedics *in vivo* data[1,2]



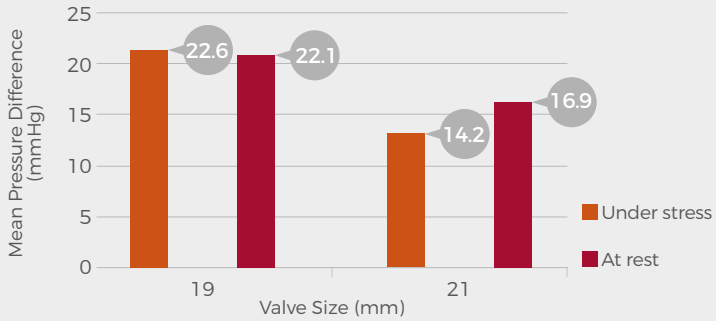


TAD: Tissue Annulus Diameter
OA: Orifice Area

In a published experience on small annuli (sizes 19 and 21), Carbomedics has shown good performance even under stress.[3]

" The result is an optimization of the discharge coefficient with exercise, indicating a good design of the moving part of the valve".[3]

Carbomedics hemodynamics at rest and under stress[3]



1. Chambers et al., Echocardiographic description of the Carbomedics bileaflet prosthetic heart valve, JACC 1993; 21(2); 398-405.
2. Bernal et al., The Carbomedics "Top Hat" Supra-annular prosthesis. - Ann Thorac Surg. 1999;67:1299-303.
3. De Paulis et al., Hemodynamic performance of small diameter Carbomedics and St. Jude valves. - J Heart Valve Dis 1996;5 (Suppl III):S339-43.

Technical claims are supported by CORCYM data on file.

Tailored ease of implant

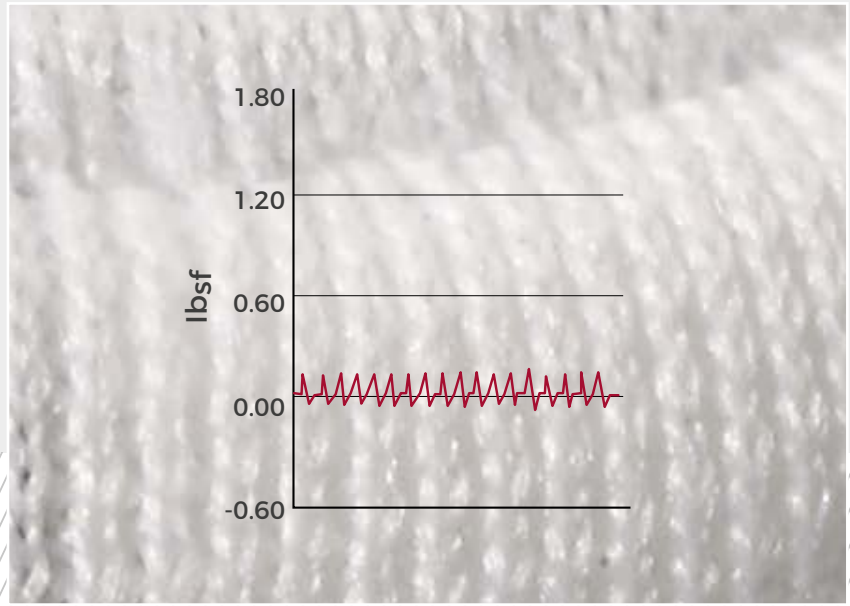
Carbomedics valves are designed for a smooth implant experience

Carbomedics sewing cuffs are optimized for ease of implant and stable seating. The Carbomedics sewing cuff requires a low force for needle penetration facilitating the suturing phase.

Most importantly, the Carbomedics sewing cuff is designed to gently conform to the tissue, thus minimizing the tension on sutures and consequently the risk of dehiscence.[1]

The broad variety of configurations was conceived to provide effective fit in any anatomical configuration.

Carbomedics Sewing Cuff Penetration Force*



* Test performed on Carbomedics Standard Mitral Model. CORCYM data on file.

1. CER-00001.

Technical claims are supported by CORCYM data on file.

Tailored solutions for every Patient and surgeon's need

Different options for your daily practice

CARBOMEDICS TOP HAT

A truly, totally supra-annular aortic prosthesis for improved hemodynamics and reduced risk of PPM*.[1,2]

It is of particular advantage also in double valve replacement, where a total supra-annular seating helps minimise the risk of interference with the mitral prosthesis.[1]

CARBOMEDICS OPTIFORM

A unique mitral prosthesis with versatile positioning to approach even challenging situations.[3]

Thanks to its flexible, generous symmetrical sewing cuff Optiform valve can conform to almost any annulus. Valve placement can be adjusted simply by varying suture entry and exit sites.

Everted Suture Technique

For atrial positioni (supra-annular), needle enters at bottom of cuff and exits at midline

For intra-annular positioning, needle enters at bottom of cuff and exits at top of cuff

For sub-annular positioning, needle enters at midline of cuff and exits at top of cuff

* Compared to non totally supra-annular models.

1. *Lundblad R et al., The Carbomedics Supraannular Top hat Valve improves prosthesis size in the Aortic Root. - J Heart Valve Dis 2001;10:196-201.*
2. *Aagard et al., Midterm Evaluation of Hemodynamics of the Top Hat Supraannular Aortic Valve. - Asian Cardiovasc Thorac Ann 2010;18:1–5.*
3. *Miyairi et al., Redo mitral valve replacement using the valve-on-valve method. - Asian Cardiovascular & Thoracic Annals 2015, Vol. 23(6) 707–709.*

Technical claims are supported by CORCYM data on file.

A complete set of mechanical heart valve solutions

Four different aortic models

Carbomedics Top Hat

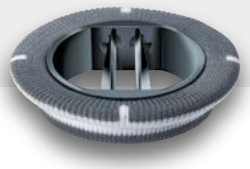
Carbomedics Standard

Carbomedics Reduced

Carbomedics Orbis

Three different mitral models

Carbomedics Standard

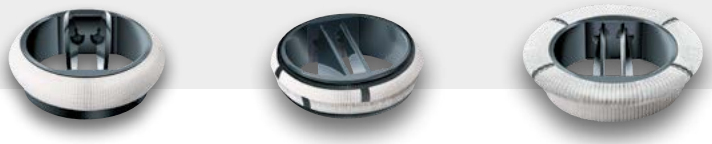


Carbomedics Optiform

Carbomedics Orbis

Small size aortic and mitral valves

Carbomedics Standard small sizes



Two different conduit models

Carbomedics
Carbo-Seal

Carbomedics
Carbo-Seal Valsalva

CARBOMEDICS™ FAMILY

The voice of experience

"We observed that the Carbomedics mechanical prosthesis had excellent durability with no structural failures, good hemodynamics, and a low incidence of TE."[1]*

"Our experience demonstrates excellent functional result of the Carbomedics valve in both mitral and aortic positions. Valve-related events were low and often caused by patient-related factors as opposed to the presence of the prosthesis."[1]*

"In our experience, structural valve failure with this device is inexistent. The Carbomedics mechanical valve is a solid choice for long-term valvular replacement."[1]*

TE: Thromboembolic Events

* CORCYM post-market surveillance classifies the incidence of valve structural failure and thromboembolic events *P*1 as improbable (10 -6 < *P*1 ≤ 10-5).

1. Bouchard et al., Twenty-Year Experience With the CarboMedics Mechanical Valve Prosthesis. - Ann Thorac Surg 2014;97:816–23.

CARBOMEDICS™ FAMILY MECHANICAL HEART VALVES

CARBOMEDICS TOP HAT

Implantation Consideration

- Totally supra-annular placement
  - provides an advantage of 1 to 2 sizes over intra-annular valves[1,2,3]
  - facilitates double valve replacement procedure[4]
- The lock wire, connecting the housing and the Titanium stiffening ring, allows for rotatability in-situ
- Three orientation markers for suture spacing
- Special sizers allow Surgeon to assess position of valve within sinus area and clearance of coronaries before implantation

Clinical Consideration

- Size upgrades provide improved valve hemodynamics*[1,2,3]
- Totally supra-annular design allows a 100% orifice to annulus match, maximazing the orifice available to blood flow[6]
- Alternative to aortic root enlargement[7]
- Low profile housing minimizes interferences with the coronary ostia
- Titanium stiffening ring minimizes the possibility of leaflet lockup or escape
- Proven reliable structural stability
- Very low valve-related adverse events[8,9]

CARBOMEDICS REDUCED
CARBOMEDICS ORBIS

Implantation Consideration

- The lock wire, connecting the housing and the Titanium stiffening ring, allows for rotatability in-situ
- Orientation markers provide easy visual suture positioning (except for Orbis)
- Carbomedics Reduced has a smaller and pliable sewing cuff with respect to the Standard model. This design was conceived for improved seating in a smaller annulus or small root.[5]

Clinical Consideration

- Low profile housing minimizes interferences with the coronary ostia
- Titanium stiffening ring minimizes the possibility of leaflet lockup or escape
- Proven reliable structural stability
- Very low valve-related adverse events[8,9]

CARBOMEDICS STANDARD

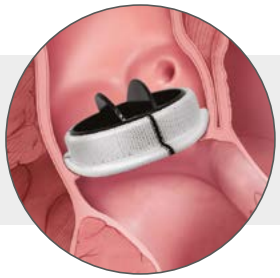
Implantation Consideration

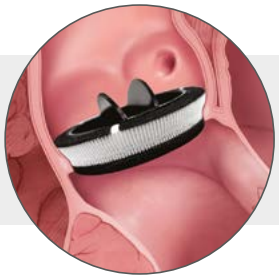
- The lock wire, connecting the housing and the Titanium stiffening ring, allows for rotatability in-situ
- Orientation markers provide easy visual suture positioning
- Generous sewing cuff conforms to annulus, designed to minimize paravalvular leaks

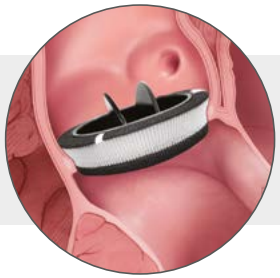
Clinical Consideration

- Low profile housing minimizes interferences with the coronary ostia
- Titanium stiffening ring minimizes the possibility of leaflet lockup or escape
- Proven reliable structural stability
- Very low valve-related adverse events[8,9]

Valve Placement *in-situ*







* Compared to non totally supra-annular models.

1. *Supra annular model as defined by International Standard for Cardiovascular implants - Cardiac valve Prostheses-Part 2. ISO 5840-2:2015(E).*
2. *Lundblad R et al., The Carbomedics Supraannular Top hat Valve improves prosthesis size in the Aortic Root. - J Heart Valve Dis 2001;10:196-201.*
3. *Aagard et al., Maximizing prosthetic valve size with the Top Hat supraannular aortic valve. - The Journal of Heart Valve Disease 2007;16:84-90.*
4. *Lundblad R et al., The Carbomedics Supraannular Top hat Valve improves prosthesis size in the Aortic Root. - J Heart Valve Dis 2001;10:196-201.*
5. *CORCYM data on file.*
6. *Aagard et al., Midterm Evaluation of Hemodynamics of the Top Hat Supraannular Aortic Valve. - Asian Cardiovasc Thorac Ann 2010;18:1-5.*
7. *Bernal et al., The Carbomedics "Top Hat" Supra-annular prosthesis. - Ann Thorac Surg. 1999;67:1299-303.*
8. *Aagard. Fifteen Years' Clinical Experience with the CarboMedics Prosthetic Heart Valve. - J Heart V Dis 2005 Jan;14(1): 82-8.*
9. *Bouchard et al., Twenty-Year Experience With the CarboMedics Mechanical Valve Prosthesis. - Ann Thorac Surg 2014;97:816-23.*

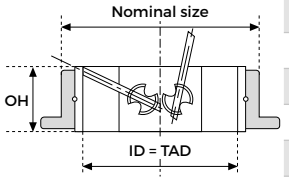
Technical claims are supported by CORCYM data on file.

CARBOMEDICS™ FAMILY

MECHANICAL
HEART VALVES

TOTALLY SUPRA-ANNULAR AORTIC VALVE Sizes 19-27 mm

Product specifications

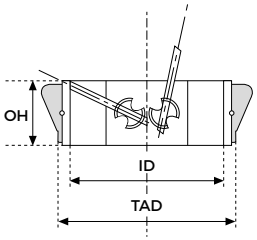


Nominal size	TAD	ID	OH	GOA	EOA	Catalog N.
19	14.7	14.7	6.2	1.59	1.0[1]	S5-019
21	16.7	16.7	6.6	2.07	1.4[2]	S5-021
23	18.5	18.5	7.3	2.56	1.9[2]	S5-023
25	20.5	20.5	7.7	3.16	2.2[2]	S5-025
27	22.5	22.5	8.4	3.84	2.9[2]	S5-027

CARBOMEDICS STANDARD

AORTIC VALVE Sizes 19-29 mm

Product specifications

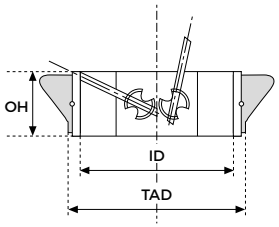


Nominal size	TAD	ID	OH	GOA	EOA[1]	Catalog N.
19	18.8	14.7	6.2	1.59	1.0	R5-019
21	20.8	16.7	6.6	2.07	1.5	R5-021
23	22.6	18.5	7.3	2.56	1.6	R5-023
25	25.0	20.5	7.7	3.16	2.0	R5-025
27	27.0	22.5	8.4	3.84	2.4	R5-027
29	29.0	24.2	8.7	4.44	2.6	R5-029

CARBOMEDICS REDUCED

AORTIC VALVE Sizes 19-29 mm

Product specifications

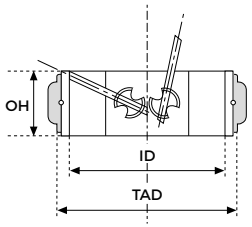


Nominal size	TAD	ID	OH	GOA	EOA[1,2]	Catalog N.
19	19.8	14.7	6.2	1.59	1.0	A5-019
21	21.8	16.7	6.6	2.07	1.5	A5-021
23	23.8	18.5	7.3	2.56	1.6	A5-023
25	25.8	20.5	7.7	3.16	2.0	A5-025
27	27.8	22.5	8.4	3.84	2.4	A5-027
29	29.8	24.2	8.7	4.44	2.6	A5-029
31	31.8	24.2	8.7	4.44	2.6	A5-031

CARBOMEDICS ORBIS

AORTIC VALVE Sizes 19-31 mm

Product specifications



Nominal size	TAD	ID	OH	GOA	EOA[1]	Catalog N.
19	18.8	14.7	6.2	1.59	1.0	A1-019
21	20.8	16.7	6.6	2.07	1.5	A1-021
23	22.6	18.5	7.3	2.56	1.6	A1-023
25	25.0	20.5	7.7	3.16	2.0	A1-025
27	27.0	22.5	8.4	3.84	2.4	A1-027
29	29.0	24.2	8.7	4.44	2.6	A1-029
31	31.0	24.2	8.7	4.44	2.6	A1-031

Legend

TAD = Tissue Annulus Diameter (mm)	EOA = In vivo Effective Orifice Area (cm²)	GOA = Geometric Orifice Area (cm²)
ID = Internal Diameter (mm)	OH = Orifice Height (mm)	

1. *Chambers et al., Echocardiographic description of the Carbomedics bileaflet prosthetic heart valve. - JACC 1993; 21(2); 398-405.*
2. *Aagard et al., Midterm Evaluation of Hemodynamics of the Top Hat Supraannular Aortic Valve. - Asian Cardiovasc Thorac Ann 2010;18:1-5.*

CARBOMEDICS STANDARD SMALL SIZES

Implantation Consideration

- Sewing cuff assembly reduces cuff size to maximize orifice area by design[1]
- The lock wire, connecting the housing and the Titanium stiffening ring, allows for rotatability in-situ
- Orientation markers provide easy visual suture positioning

Clinical Consideration

- Fits where other Carbomedics valves will not
- Titanium stiffening ring minimizes the possibility of leaflet lockup or escape
- Proven reliable structural stability

Valve Placement *in-situ*

CARBOMEDICS STANDARD SMALL SIZES

Implantation Consideration

- Sewing cuff assembly reduces cuff size to maximize orifice area by design[1]
- The lock wire, connecting the housing and the Titanium stiffening ring, allows for rotatability in-situ
- Orientation markers provide easy visual suture positioning

Clinical Consideration

- Fits where other Carbomedics valves will not
- Titanium stiffening ring minimizes the possibility of leaflet lockup or escape
- Proven reliable structural stability

Valve Placement *in-situ*

1. CORCYM data on file.

Technical claims are supported by CORCYM data on file.

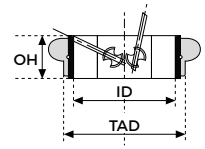

Size 16

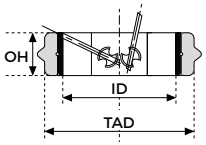

Size 18

CARBOMEDICS STANDARD SMALL SIZES

AORTIC VALVES Sizes 16 and 18 mm

Product specifications





Nominal size	TAD	ID	OH	GOA	EOA[1]	Catalog N.
16	16.2	14.7	6.2	1.59	1	A5-016
18	18.8	14.7	6.2	1.59	1	A5-018


Size 16

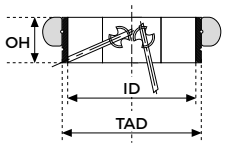

Size 18

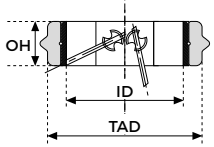

Size 21

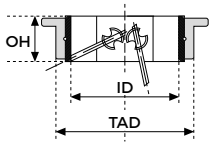
CARBOMEDICS STANDARD SMALL SIZES

MITRAL VALVES Sizes 16, 18 and 21 mm

Product specifications







Nominal size	TAD	ID	OH	GOA	Catalog N.
16	16.2	14.7	6.2	1.59	M7-016
18	18.8	14.7	6.2	1.59	M7-018
21	21.8	16.7	6.6	2.07	M7-021

Legend

TAD = Tissue Annulus Diameter (mm)	EOA = In vivo Effective Orifice Area (cm^2)	GOA = Geometric Orifice Area (cm^2)
ID = Internal Diameter (mm)	OH = Orifice Height (mm)	

1. *Chambers et al., Echocardiographic description of the Carbomedics bileaflet prosthetic heart valve. - JACC 1993; 21(2): 398-405.*

CARBOMEDICS STANDARD

Implantation Consideration

- Generous sewing cuff conforms to annulus, designed to minimize paravalvular leaks
- The lock wire, connecting the housing and the Titanium stiffening ring, allows for rotatability in-situ
- Orientation markers provide easy visual suture positioning

Clinical Consideration

- Low-profile pivot design minimizes protrusion into low-flow atrial area, reducing potential thrombus formation
- Titanium stiffening ring minimizes the possibility of leaflet lockup or escape
- Proven reliable structural stability
- Very low valve-related adverse events[3,4]

Valve Placement *in-situ*

CARBOMEDICS OPTIFORM
CARBOMEDICS ORBIS

Implantation Consideration

- Symmetrical cuff design allows valve to be placed in a supraannular, intra-annular or subannular position simply by varying suture entry and exit sites[1,2]
- Flexible, generous cuff easily conforms to difficult Patient annular anatomy[1,2]
- The lock wire, connecting the housing and the Titanium stiffening ring, allows for rotatability in-situ
- Orientation markers provide easy visual suture positioning (Carbomedics Optiform only)

Clinical Consideration

- Variable valve placement allows Surgeon to choose best valve position for each Patient
- Titanium stiffening ring minimizes the possibility of leaflet lockup or escape
- Proven reliable structural stability
- Very low valve-related adverse events[3,4]

Valve Placement *in-situ*

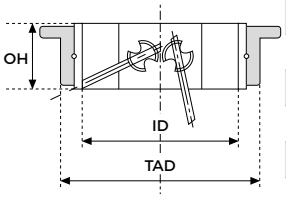
1. *Miyairi et al., Redo mitral valve replacement using the valve-on-valve method. - Asian Cardiovascular & Thoracic Annals 2015, Vol. 23(6) 707–709.*
2. *CORCYM data on file.*
3. *Aagard. Fifteen Years' Clinical Experience with the CarboMedics Prosthetic Heart Valve. - J Heart V Dis 2005 Jan;14(1): 82-8.*
4. *Bouchard et al., Twenty-Year Experience With the CarboMedics Mechanical Valve Prosthesis. - Ann Thorac Surg 2014;97:816–23.*

Technical claims are supported by CORCYM data on file.

CARBOMEDICS STANDARD

MITRAL VALVE Sizes 23-33 mm

Product specifications

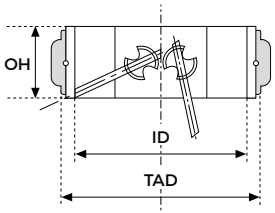


Nominal size	TAD	ID	OH	GOA	Catalog N.
23	23.8	18.5	7.3	2.56	M7-023
25	25.8	20.5	7.7	3.16	M7-025
27	27.8	22.5	8.4	3.84	M7-027
29	29.8	24.2	8.7	4.44	M7-029
31	31.8	24.2	8.7	4.44	M7-031
33	33.8	24.2	8.7	4.44	M7-033

CARBOMEDICS ORBIS

MITRAL VALVE Sizes 21-33 mm

Product specifications

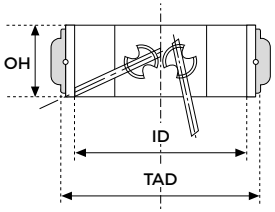


Nominal size	TAD	ID	OH	GOA	Catalog N.
21	20.8	16.7	6.6	2.07	M2-021
23	22.6	18.5	7.3	2.56	M2-023
25	25.0	20.5	7.7	3.16	M2-025
27	27.0	22.5	8.4	3.84	M2-027
29	29.0	24.2	8.7	4.44	M2-029
31	31.0	24.2	8.7	4.44	M2-031
33	33.0	24.2	8.7	4.44	M2-033

CARBOMEDICS OPTIFORM

MITRAL VALVE Sizes 23-33 mm

Product specifications



Nominal size	TAD	ID	OH	GOA	Catalog N.
23	22.6	18.5	7.3	2.56	F7-023
25	25.0	20.5	7.7	3.16	F7-025
27	27.0	22.5	8.4	3.84	F7-027
29	29.0	24.2	8.7	4.44	F7-029
31	31.0	24.2	8.7	4.44	F7-031
33	33.0	24.2	8.7	4.44	F7-033

Legend

TAD = Tissue Annulus Diameter (mm)	OH = Orifice Height (mm)
ID = Internal Diameter (mm)	GOA = Geometric Orifice Area (cm²)

CARBOMEDICS CARBO-SEAL VALSALVA

Implantation Consideration

- Vertical orientation of sinus pleats facilitates coronary anastomosis[1]
- Graft material resists fraying and quickly seals suture holes, minimizing bleeding[2]
- Easier handling and suturing in comparison to bulkier velour materials[3]
- Ultra-low porosity fabric and gelatin sealing result in less leakage, weeping and blushing[2]
- Pliable, cork-shaped sewing cuff conforms to annulus, designed to minimize potential paravalvular leaks
- Titanium stiffening ring allows valve rotatability in-situ
- Orientation markers provide easy visual suture positioning

Clinical Consideration

- Graft is infused with minimally crosslinked gelatin that does not alter the healing process, encouraging a secure neo-intimal attachment with reduced inflammatory response[4]
- Gelatin hydrolyzes within 14 days[5]
- Sinus of Valsalva reproduces the native sinus, reducing required dissection of and stress on the coronary anastomoses[1]
- Sinus design encourages natural formation of systolic vortex[6]
- Full-sized standard aortic valve provides favorable hemodynamics[7]
- Very low rate of thromboembolic events[8,9]
- Titanium stiffening ring minimizes the possibility of leaflet lockup or escape

CARBOMEDICS CARBO-SEAL

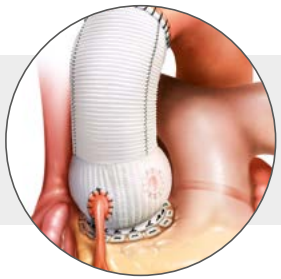
Implantation Consideration

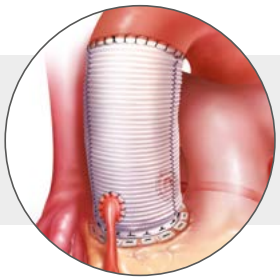
- Pliable, cork-shaped sewing cuff conforms to annulus, designed to minimize potential paravalvular leaks
- Graft material resists fraying and quickly seals suture holes, minimizing bleeding[2]
- Easier handling and suturing in comparison to bulkier velour materials[3]
- Ultra-low porosity fabric and gelatin sealing result in less leakage, weeping and blushing[2]
- Titanium stiffening ring allows rotatability in-situ
- Orientation markers provide easy visual suture positioning

Clinical Consideration

- Graft is infused with minimally crosslinked gelatin that does not alter the healing process, encouraging a secure neo-intimal attachment with reduced inflammatory response[4]
- Collagen gel hydrolyzes within 14 days
- Full-sized standard aortic valve provides favorable hemodynamics[7]
- Very low rate of thromboembolic events[8,9]
- Titanium stiffening ring minimizes the possibility of leaflet lockup or escape

Valve Placement *in-situ*



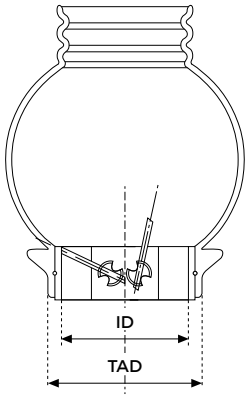


1. *De Paulis, et al., One-year appraisal of a new aortic root conduit with sinuses of Valsalva. - J Thorac Cardiovasc Surg 2002;123:33-9.*
2. *CORCYM data on file.*
3. *Kadoba et al., Experimental comparison of albumin-sealed and gelatin-sealed knitted Dacron conduits. - J Thorac and Cardiovasc Surg 1992;103:1059-67.*
4. *Drury et al., Experimental and Clinical Experience with a Gelatin Impregnated Dacron Prosthesis. - Ann Vasc Surg, 1987, 7, 542-547.*
5. *Cavallaro, A., Sciacca, V., Cisternino, S., Di Marzo, L., Mingoli, A., Abrize, C., Gallo, P., Pollock, J.G., Maini, R., 1986. Pretreatment with gelatin of Dacron Grafts. Experimental Research. Policlinico Sez Chir. Vol. 93 pp. 275-283 [article in italian].*
6. *De Paulis et al., A New Aortic Dacron Conduit for Surgical Treatment of Aortic Root Pathology. - Ital Heart J 2000, 1 (7), 457-463.*
7. *Bouchard et al., Twenty-Year Experience With the CarboMedics Mechanical Valve Prosthesis. - Ann Thorac Surg 2014;97:816–23.*
8. *SM. Langley et al., Replacement of the proximal aorta and aortic valve using a composite bileaflet prosthesis and gelatin-impregnated polyester graft (Carbo-seal): early results in 143 patients. - J Thorac Cardiovasc Surg 1999;118:1014-20*
9. *De Paulis et al., Opening and closing characteristics of the aortic valve after valve-sparing procedure usign a new aortic root conduit. - Ann Thorac Surg 2001;72:487-494.*

Technical claims are supported by CORCYM data on file.

CARBOMEDICS CARBO-SEAL VALSALVA

ASCENDING AORTIC PROSTHESIS (AAP) Sizes 21-29 mm

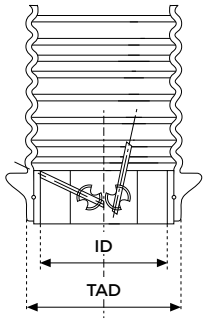


Product specifications

Nominal size	TAD	ID	GOA	Graft ID	Catalog N.
21	21.8	16.7	2.07	24	CP-021
23	23.8	18.5	2.56	26	CP-023
25	25.8	20.5	3.16	28	CP-025
27	27.8	22.5	3.84	30	CP-027
29	29.8	24.2	4.44	32	CP-029

CARBOMEDICS CARBO-SEAL

ASCENDING AORTIC PROSTHESIS (AAP) Sizes 21-33 mm



Product specifications

Nominal size	TAD	ID	GOA	Graft ID	Catalog N.
21	21.8	16.7	2.07	24	AP-021
23	23.8	18.5	2.56	26	AP-023
25	25.8	20.5	3.16	28	AP-025
27	27.8	22.5	3.84	30	AP-027
29	29.8	24.2	4.44	32	AP-029
31	31.8	24.2	4.44	34	AP-031
33	33.8	24.2	4.44	34	AP-033

Legend

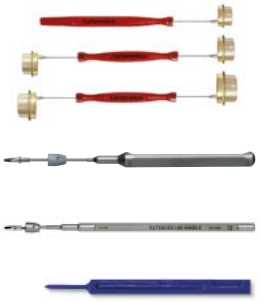
TAD = Tissue Annulus Diameter (mm) ID = Internal Diameter (mm) GOA = Geometric Orifice Area (cm^2)

Aortic mechanical valves ACCESSORIES

CARBOMEDICS TOP HAT

Aortic Mechanical Bileaflet Valve

Article	Code	Description
Empty tray	TR-101	1 empty tray
Sizer set	SAS-200	3 sizers 19mm, 21-23mm, 25-27mm
Uni Handle	ICV0664	1 Universal Bendable Handle
Extended Uni Handle	ICV1342	1 Universal Extended Bendable Handle
Occluder tester	VT-100	10 disposable occluder tester (provided sterile)



CARBOMEDICS REDUCED, ORBIS, STANDARD

Aortic Mechanical Bileaflet Valve

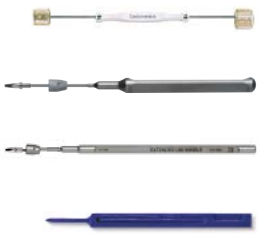
Article	Code	Description
Empty tray	TR-101	1 empty tray
Sizer set	VS-200	4 sizers 19-21mm, 23-25mm 27-29mm, 31-33mm
Uni Handle	ICV0664	1 Universal Bendable Handle
Extended Uni Handle	ICV1342	1 Universal Extended Bendable Handle
Occluder tester	VT-100	10 disposable occluder tester (provided sterile)

Small size Mechanical Valves ACCESSORIES

CARBOMEDICS STANDARD SMALL SIZES

Aortic Mechanical Bileaflet Valve

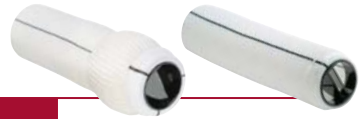
Article	Code	Description
Empty tray	TR-101	1 empty tray
Sizer	VS2-1618	1 sizer (16-18mm)
Uni Handle	ICV0664	1 Universal Bendable Handle
Extended Uni Handle	ICV1342	1 Universal Extended Bendable Handle
Occluder tester	VT-100	10 disposable occluder tester (provided sterile)



Aortic mechanical conduits ACCESSORIES

CARBOMEDICS CARBO-SEAL VALSALVA, CARBO-SEAL

Aortic Mechanical Conduit



Article	Code	Description
Empty tray	TR-101	1 empty tray
Sizer set	VS-200	4 sizers 19-21mm, 23-25mm 27-29mm, 31-33mm
Rotators set	AR-150	6 aortic rotators
Occluder tester	VT-100	10 disposable occluder tester (provided sterile)

Mitral Mechanical Valve ACCESSORIES

CARBOMEDICS OPTIFORM, ORBIS, STANDARD

Mitral Mechanical Bileaflet Valve

Article	Code	Description
Empty tray	TR-101	1 empty tray
Sizer set	VS-200	4 sizers 19-21mm, 23-25mm 27-29mm, 31-33mm
Uni Handle	ICV0664	1 Universal Bendable Handle
Extended Uni Handle	ICV1342	1 Universal Extended Bendable Handle
Occluder tester	VT-100	10 disposable occluder tester (provided sterile)

CARBOMEDICS STANDARD SMALL SIZES

Mitral Mechanical Bileaflet Valve

Article	Code	Description
Empty tray	TR-101	1 empty tray
Sizer	VS2-1618	1 sizer (16-18mm)
Sizer set	VS-200	4 sizers 19-21mm, 23-25mm 27-29mm, 31-33mm
Uni Handle	ICV0664	1 Universal Bendable Handle
Extended Uni Handle	ICV1342	1 Universal Extended Bendable Handle
Occluder tester	VT-100	10 disposable occluder tester (provided sterile)

CARBOMEDICS™ FAMILY

MECHANICAL
HEART VALVES

INTENDED USE/INDICATIONS

Europe, Australia: The Carbomedics Prosthetic Heart Valve is intended for use as a replacement valve in patients with diseased, damaged, or malfunctioning aortic or mitral heart valve.
The Carbomedics Prosthetic Heart Valve Aortic/Mitral models, respectively, are indicated for use in patients suffering from aortic/mitral valvular heart disease, that is a condition involving obstruction of the aortic/mitral heart valve or stenosis; leakage of the aortic/mitral valve, known as regurgitation, incompetence, or insufficiency; and combinations of the two or patients with a previously implanted aortic/mitral valve prosthesis that is no longer functioning adequately and requires replacement.

US, Canada: The Carbomedics Prosthetic Heart Valves are indicated as a replacement for human cardiac valves that are malfunctioning as a result of acquired or congenital disease, or as a replacement of a previously implanted prosthesis.

KEY CONTRAINDICATIONS

There are no absolute contraindications to the use of the Carbomedics Prosthetic Heart Valve. The mechanical heart valves are contraindicated or difficult to apply in patients unable to tolerate long term anticoagulation therapy or for whom this type of therapy is difficult to carry out.

KEY WARNINGS

For single use only. Safety and effectiveness of the Carbomedics valve has not been demonstrated for valve replacement in the pulmonic and tricuspid positions. Handle the valve only with accessories provided by the manufacturer specifically for the Carbomedics valve. Only use sizers provided by the manufacturer specifically for the Carbomedics valve.

TOP POTENTIAL SIDE EFFECTS

The risks or potential adverse events associated with cardiac valve replacement with a prosthetic mechanical heart valve include: cardiac arrhythmias, death, endocarditis, hemolysis, anti-coagulation related hemorrhage, leaflet entrapment by tissue ingrowth or impingement on anatomic structures, intravalvular and/or paravalvular leak, prosthetis thrombosis, thromboembolism, structural valve deterioration.

MRI conditional

For professional use. Please contact us through our website to receive instructions for use containing full prescribing information, including indications, contraindications, warnings, precautions and adverse events. Not approved in all geographies. Consult your labeling.

CORCYM
WE TAKE LIFE TO HEART

Manufactured by:

Sorin Group Italia Srl
Via per Crescentino sn
13040 Saluggia (VC) Italy
Tel: +39 0161 487800

CE 0123

corcym
.com

CC-MK-00003 A

CORCYM
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DICHIARAZIONE DI CONFORMITÀ CE
EC DECLARATION OF CONFORMITY

La sottoscritta **Corcym S.r.l.** (Via Crescentino sn, 13040 Saluggia, VC - Italia) dichiara sotto la propria responsabilità di Fabbricante che i prodotti sotto elencati sono conformi alle disposizioni applicabili della Direttiva del Consiglio 93/42/CEE e del Regolamento (UE) della Commissione no. 207/2012.

We, the undersigned ***Corcym S.r.l.*** *(Via Crescentino sn, 13040 Saluggia, VC - Italy) declare under our sole responsibility as Manufacturer that the products identified below conform to the relevant provisions of Council Directive 93/42/EEC and Commission Regulation (EU) no. 207/2012.*

Identificazione prodotto *Product identification*			
Prodotto *Product*	**Taglia** *Size*	**Codice prodotto (REF)** *Catalogue number (REF)*	**Classe** *Class*
Carbomedics Standard Aortic	16	A5-016	III
	18	A5-018	
	19	A5-019	
	21	A5-021	
	23	A5-023	
	25	A5-025	
	27	A5-027	
	29	A5-029	
	31	A5-031	
Carbomedics Standard Mitral	16	M7-016	III
	18	M7-018	
	21	M7-021	
	23	M7-023	
	25	M7-025	
	27	M7-027	
	29	M7-029	
	31	M7-031	
	33	M7-033	
Carbomedics Reduced Aortic	19	R5-019	III
	21	R5-021	
	23	R5-023	
	25	R5-025	
	27	R5-027	
	29	R5-029	
Carbomedics Supra-Annular Aortic (Top Hat)	19	S5-019	III
	21	S5-021	
	23	S5-023	
	25	S5-025	
	27	S5-027	

(cont.)

CORCYM SRL
Sede Legale
Via Benigno Crespi 17 - 20159 Milano - Italy

Sede Amministrativa
Via Benigno Crespi 17 - 20159 Milano - Italy
Via per Crescentino sn - 13040 Saluggia (VC) Italy
Tel.+39 0161 487.1 - Fax +39 0161 487.545

Stabilimento
Via Crescentino sn - 13040 Saluggia (VC) Italy

PEC: CORCYM@LEGALMAIL.IT

Capitale Sociale: € 2.000.000,00
R.E.A. MILANO 2608814
Registro Imprese di Milano N.11515960968
Cod. Fiscale / Part. IVA 11515960968

ISO Code: IT11515960968
corcym.com

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Identificazione prodotto ***Product Identification***			
Prodotto *Product*	**Taglia** *Size*	**Codice prodotto (REF)** *Catalogue number (REF)*	**Classe** *Class*
Carbomedics Orbis Aortic	19	A1-019	III
	21	A1-021	
	23	A1-023	
	25	A1-025	
	27	A1-027	
	29	A1-029	
	31	A1-031	
Carbomedics Orbis Mitral	21	M2-021	III
	23	M2-023	
	25	M2-025	
	27	M2-027	
	29	M2-029	
	31	M2-031	
	33	M2-033	
Carbomedics Optiform Mitral	21	F7-021	III
	23	F7-023	
	25	F7-025	
	27	F7-027	
	29	F7-029	
	31	F7-031	
	33	F7-033	

Informazioni relative alla valutazione della conformità ***Conformity assessment information***		
Organismo Notificato *Notified Body*	**Procedura di valutazione conformità** *Conformity assessment procedure*	**Numero certificati CE** *CE Certificates number*
TÜV SÜD Product Service GmbH (0123) Ridlerstr. 65, D-80339 München, GERMANY	Dichiarazione di Conformità CE di cui all' Allegato II, Direttiva 93/42/CEE (Sistema completo di assicurazione di qualità) *EC Declaration of Conformity set out in Annex II, Directive 93/42/EEC (Full Quality Assurance)*	- Annex II section 4: G7 001664 0035 Rev. 01 Valid until: 2024-05-26 - Annex II excluding section 4: G1 001664 0038 Rev.01 Valid until: 2024-05-26

La presente Dichiarazione di Conformità è valida per i dispositivi prodotti presso l'officina sita in Via Crescentino sn, 13040 Saluggia, VC – Italia e descritti nel Technical File TF-03.

This Declaration of Conformity is valid for the medical devices manufactured in the facility of Via Crescentino sn, 13040 Saluggia, VC – Italy and described in the Technical File TF-03.

SOCIETATEA CU RĂSPUNDERE LIMITATĂ
S.R.L.
IDNO 1010800028048
REPUBLICA MOLDOVA

La presente Dichiarazione di Conformità è valida a partire dalla data di firma e fino alla prima data di scadenza dei certificati sopra indicati.

This Declaration of Conformity is valid from the signature date until the earliest expiry date of the certificates identified above.

Saluggia, June 1st, 2021

Adelina Chiaravalloti

Director, Regulatory Affairs and Clinical Evaluation
Corcym S.r.l.

ZERTIFIKAT ◆ CERTIFICATE ◆ 認證書 ◆ СЕРТИФИКАТ ◆ CERTIFICADO ◆ CERTIFICAT

Benannt durch/Designated by
Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten
www.zlg.de
ZLG-BS-244.10.08

Product Service

EC Certificate

Full Quality Assurance System
Directive 93/42/EEC on Medical Devices (MDD), Annex II excluding (4)
(Devices in Class IIa, IIb or III)

No. G1 001664 0038 Rev. 01

Manufacturer:

Corcym S.r.l.
Via Crescentino sn
13040 Saluggia (VC)
ITALY

Product Category(ies): **Mechanical Heart Valves**

The Certification Body of TÜV SÜD Product Service GmbH declares that the aforementioned manufacturer has implemented a quality assurance system for design, manufacture and final inspection of the respective devices / device categories in accordance with MDD Annex II.
This quality assurance system conforms to the requirements of this Directive and is subject to periodical surveillance. For marketing of class III devices an additional Annex II (4) certificate is mandatory. All applicable requirements of the testing and certification regulation of TÜV SÜD Group have to be complied with. For details and certificate validity see: www.tuvsud.com/ps-cert?q=cert:G1 001664 0038 Rev. 01

Report No.: ITA1663134

Valid from: 2021-05-25
Valid until: 2024-05-26

Date, 2021-05-10

Christoph Dicks
Head of Certification/Notified Body

SOCIETATEA CU RĂSPUNDERE LIMITATĂ
BioSistem SRL
IDNO 1010600028048
REPUBLICA MOLDOVA

TÜV SÜD Product Service GmbH is Notified Body with identification no. 0123

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ZLG-BS-244.10.08

TÜV SÜD Product Service

EC Certificate

EC Design-Examination Certificate
Directive 93/42/EEC on Medical Devices (MDD), Annex II (4)
(Devices in Class III)

No. G7 001664 0035 Rev. 01

Manufacturer: **Corcym S.r.l.**
Via Crescentino sn
13040 Saluggia (VC)
ITALY

Product: **Heart Valves**

The Certification Body of TÜV SÜD Product Service GmbH declares that a design examination has been carried out on the respective devices in accordance with MDD Annex II (4). The design of the devices conforms to the requirements of this Directive. For marketing of these devices an additional Annex II certificate is mandatory. All applicable requirements of the testing and certification regulation of TÜV SÜD Group have to be complied with. For details and certificate validity see:
www.tuvsud.com/ps-cert?q=cert:G7 001664 0035 Rev. 01

Report no.: 713206835

Valid from: 2021-05-25
Valid until: 2024-05-26

Date, 2021-05-10

Christoph Dicks
Head of Certification/Notified Body

SOCIETATEA CU RĂSPUNDERE LIMITATĂ
S.R.L.
IDNO 1010800028048
REPUBLICA MOLDOVA

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TÜV SÜD Product Service

EC Certificate

EC Design-Examination Certificate
Directive 93/42/EEC on Medical Devices (MDD), Annex II (4)
(Devices in Class III)

No. G7 001664 0035 Rev. 01

Model(s): Carbomedics Mechanical Bileaflet Heart

Parameters:

Product Name	Size	Product codes
Carbomedics Standard Aortic	16	A5-016
	18	A5-018
	19	A5-019
	21	A5-021
	23	A5-023
	25	A5-025
	27	A5-027
	29	A5-029
	31	A5-031
Carbomedics Standard Mitral	16	M7-016
	18	M7-018
	21	M7-021
	23	M7-023
	25	M7-025
	27	M7-027
	29	M7-029
	31	M7-031
	33	M7-033
Carbomedics Reduced Aortic	19	R5-019
	21	R5-021
	23	R5-023
	25	R5-025
	27	R5-027
	29	R5-029
Carbomedics Supra-Annular Aortic	19	S5-019
	21	S5-021
	23	S5-023
	25	S5-025
	27	S5-027
Carbomedics Orbis Aortic	19	A1-019
	21	A1-021
	23	A1-023

TÜV SÜD Product Service GmbH is Notified Body with identification no. 0123

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SOCIETATEA CU RĂSPUNDERE LIMITATĂ Bios'stem S.R.L. IDNO 1010800028046 REPUBLICA MOLDOVA

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TÜV SÜD Product Service

EC Certificate

EC Design-Examination Certificate
Directive 93/42/EEC on Medical Devices (MDD), Annex II (4)
(Devices in Class III)

No. G7 001664 0035 Rev. 01

	25	A1-025
	27	A1-027
	29	A1-029
	31	A1-031
Carbomedics Orbis Mitral	21	M2-021
	23	M2-023
	25	M2-025
	27	M2-027
	29	M2-029
	31	M2-031
	33	M2-033
Carbomedics Optiform Mitral	21	F7-021
	23	F7-023
	25	F7-025
	27	F7-027
	29	F7-029
	31	F7-031
	33	F7-033

SOCIETATEA CU RĂSPUNDERE LIMITATĂ Biotistem S.R.L. IDNO 1010600028048 REPUBLICA MOLDOVA

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DICHIARAZIONE DI CONFORMITÀ CE
EC DECLARATION OF CONFORMITY

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Identificazione prodotto *Product identification*				
Prodotto *Product*	**Taglia** *Size*	**Codice prodotto (REF)** *Catalogue number (REF)*	**Codice d'ordine** *Ordering code*	**Classe** *Class*
Bicarbon Fitline LFA Aortic	19	ART19LFA	ICV0917	III
	21	ART21LFA	ICV0918	
	23	ART23LFA	ICV0919	
	25	ART25LFA	ICV0920	
	27	ART27LFA	ICV0921	
	29	ART29LFA	ICV0922	
	31	ART31LFA	ICV0923	
Bicarbon Fitline LFM Mitral	19	MTR19LFM	ICV0924	III
	21	MTR21LFM	ICV0925	
	23	MTR23LFM	ICV0926	
	25	MTR25LFM	ICV0927	
	27	MTR27LFM	ICV0928	
	29	MTR29LFM	ICV0929	
	31	MTR31LFM	ICV0930	
	33	MTR33LFM	ICV0931	
Bicarbon Slimline LSA Aortic	17	ART17LSA	ICV0934	III
	19	ART19LSA	ICV0935	
	21	ART21LSA	ICV0936	
	23	ART23LSA	ICV0937	
	25	ART25LSA	ICV0938	
	27	ART27LSA	ICV0939	
Bicarbon Overline Aortic	16	ART16LOV	ICV0870	III
	18	ART18LOV	ICV0871	
	20	ART20LOV	ICV0872	
	22	ART22LOV	ICV0873	
	24	ART24LOV	ICV0874	

SOCIETATEA CU RĂSPUNDERE LIMITATĂ S.R.L. BioSistem MLD IDNO 1004600028048 REPUBLICA MOLDOVA

CORCYM SRL
Sede Legale
Via Benigno Crespi 17 – 20159 Milano – Italy

Sede Amministrativa
Via Benigno Crespi 17 – 20159 Milano – Italy
Via per Crescentino sn – 13040 Saluggia (VC) Italy

Stabilimento
Via Crescentino sn – 13040 Saluggia (VC) Italy

PEC: CORCYM@LEGALMAIL.IT

Capitale Sociale: € 2.000.000,00
R.E.A. MILANO 2608814
Registro Imprese di Milano N.11515960968
Cod. Fiscale / Part. IVA 11515960968

ISO Code: IT11515960968
corcym.com

CORCYM
WE TAKE LIFE TO HEART

Informazioni relative alla valutazione della conformità *Conformity assessment information*		
Organismo Notificato *Notified Body*	**Procedura di valutazione conformità** *Conformity assessment procedure*	**Numero certificati CE** *CE Certificates number*
TÜV SÜD Product Service GmbH (0123) Ridlerstr. 65, D-80339 München, GERMANY	Dichiarazione di Conformità CE di cui all' Allegato II, Direttiva 93/42/CEE (Sistema completo di assicurazione di qualità) *EC Declaration of Conformity set out in Annex II, Directive 93/42/EEC (Full Quality Assurance)*	- Annex II section 4: G7 001664 0034 Rev. 01 Valid until: 2024-05-26 - Annex II excluding section 4: G1 001664 0038 Rev.01 Valid until: 2024-05-26

La presente Dichiarazione di Conformità è valida per i dispositivi prodotti presso l'officina sita in Via Crescentino sn, 13040 Saluggia, VC – Italia e descritti nel Technical File TF-08.

This Declaration of Conformity is valid for the medical devices manufactured in the facility of Via Crescentino sn, 13040 Saluggia, VC – Italy and described in the Technical File TF-08.

La presente Dichiarazione di Conformità è valida a partire dalla data di firma e fino alla prima data di scadenza dei certificati sopra indicati.

This Declaration of Conformity is valid from the signature date until the earliest expiry date of the certificates identified above.

Saluggia, June 1st, 2021

Adelina Chiaravalloti
Director, Regulatory Affairs and Clinical Evaluation
Corcym S.r.l.

SOCIETATEA CU RĂSPUNDERE LIMITATĂ S.R.L. BioSistem MLD IDNO 1010 REPUBLICA MOLDOVA

ZERTIFIKAT ◆ CERTIFICATE ◆ 認證書 ◆ СЕРТИФИКАТ ◆ CERTIFICADO ◆ CERTIFICAT

Benannt durch/Designated by
Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten
www.zlg.de
ZLG-BS-244.10.08

TÜV SÜD Product Service

EC Certificate

EC Design-Examination Certificate
Directive 93/42/EEC on Medical Devices (MDD), Annex II (4)
(Devices in Class III)

No. G7 001664 0034 Rev. 01

Manufacturer: **Corcym S.r.l.**
Via Crescentino sn
13040 Saluggia (VC)
ITALY

Product: **Heart Valves**
Sorin Mechanical Heart Valves

The Certification Body of TÜV SÜD Product Service GmbH declares that a design examination has been carried out on the respective devices in accordance with MDD Annex II (4). The design of the devices conforms to the requirements of this Directive. For marketing of these devices an additional Annex II certificate is mandatory. All applicable requirements of the testing and certification regulation of TÜV SÜD Group have to be complied with. For details and certificate validity see:
www.tuvsud.com/ps-cert?q=cert:G7 001664 0034 Rev. 01

Report no.: 713206835

Valid from: 2021-05-25
Valid until: 2024-05-26

Date, 2021-05-10

Christoph Dicks
Head of Certification/Notified Body

TÜV SÜD Product Service GmbH is Notified Body with identification no. 0123

TÜV SÜD Product Service GmbH • Certification Body • Ridlerstraße 65 • 80339 Munich • Germany

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TÜV SÜD Product Service

EC Certificate

EC Design-Examination Certificate
Directive 93/42/EEC on Medical Devices (MDD), Annex II (4)
(Devices in Class III)

No. G7 001664 0034 Rev. 01

Model(s):

Bicarbon Fitline
Bicarbon Slimline
Bicarbon Overline

Parameters:

Model Name	Product codes
Bicarbon Fitline LFA Aortic	ICV0917/ART19LFA
	ICV0918/ART21LFA
	ICV0919/ART23LFA
	ICV0920/ART25LFA
	ICV0921/ART27LFA
	ICV0922/ART29LFA
	ICV0923/ART31LFA
Bicarbon Fitline LFM Mitral	ICV0924/MTR19LFM
	ICV0925/MTR21LFM
	ICV0926/MTR23LFM
	ICV0927/MTR25LFM
	ICV0928/MTR27LFM
	ICV0929/MTR29LFM
	ICV0930/MTR31LFM
	ICV0931/MTR33LFM
Bicarbon Slimline LSA Aortic	ICV0934/ART17LSA
	ICV0935/ART19LSA
	ICV0936/ART21LSA
	ICV0937/ART23LSA
	ICV0938/ART25LSA
	ICV0939/ART27LSA
Bicarbon Overline Aortic	ICV0870/ART16LOV
	ICV0871/ART18LOV
	ICV0872/ART20LOV
	ICV0873/ART22LOV
	ICV0874/ART24LOV

SOCIETATEA CU RĂSPUNDERE LIMITATĂ S.R.L. Biosistem MLD IDNO 1010600028048 REPUBLICA MOLDOVA

TÜV SÜD Product Service GmbH is Notified Body with identification no. 0123

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www.zlg.de
ZLG-BS-244.10.08

TÜV SÜD Product Service

EC Certificate

Full Quality Assurance System
Directive 93/42/EEC on Medical Devices (MDD), Annex II excluding (4)
(Devices in Class IIa, IIb or III)

No. G1 001664 0038 Rev. 01

Manufacturer:

Corcym S.r.l.
Via Crescentino sn
13040 Saluggia (VC)
ITALY

Product Category(ies): **Mechanical Heart Valves**

The Certification Body of TÜV SÜD Product Service GmbH declares that the aforementioned manufacturer has implemented a quality assurance system for design, manufacture and final inspection of the respective devices / device categories in accordance with MDD Annex II. This quality assurance system conforms to the requirements of this Directive and is subject to periodical surveillance. For marketing of class III devices an additional Annex II (4) certificate is mandatory. All applicable requirements of the testing and certification regulation of TÜV SÜD Group have to be complied with. For details and certificate validity see: www.tuvsud.com/ps-cert?q=cert:G1 001664 0038 Rev. 01

Report No.: ITA1663134

Valid from: 2021-05-25
Valid until: 2024-05-26

Date, 2021-05-10

Christoph Dicks
Head of Certification/Notified Body

SOCIETATEA CU RĂSPUNDERE LIMITATĂ S.R.L. Biosistem IDNO 1010600028048 REPUBLICA MOLDOVA

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ARTIVION
Formerly CryoLife | Jotec
artivion.com

EU DECLARATION OF CONFORMITY

according to *Annex IV of the Medical Device Regulation (EU) 2017/ 745*

Manufacturer's Name:	Artivion, Inc. (formerly CryoLife)
SRN:	US-MF-000015763
Business Address:	1655 Roberts Blvd, NW Kennesaw, Georgia 30144 United States of America
Authorized European Representative:	Jotec GmbH
SRN:	DE-AR -000006801
Business Address:	Lotzenäcker 23 72379 Hechingen, Germany
Object of this Declaration:	BioGlue® Surgical Adhesive (See Attachment #1)
Intended Purpose/ Indications for Use:	BioGlue® Surgical Adhesive is indicated for use as an adjunct to standard methods of surgical repair (such as sutures, staples, and/or patches) to adhere, seal, and/ or reinforce soft tissue. Indicated soft tissues are cardiac, vascular, pulmonary, and dural.
Classification:	Class III, according to 2017/745 Annex VIII, Chapter III, Rules 8 (long-term surgically invasive implantable device intended to be used in direct contact with the heart, the central circulatory system or the central nervous system, and have a biological effect or are wholly or mainly absorbed) and 18 (utilizes tissues or cells of human or animal origin, or their derivatives, which are non-viable or rendered non-viable)
MDR Codes:	Design and intended purpose: MDN 1101 Specific characteristics: MDS 1001, MDS 1005 Technologies or processes: MDT 2008, MDT 2009, MDT 2011
Notified Body:	DEKRA Certification GmbH, Handwerkstr. 15, 70565 Stuttgart, Germany, ID No. 0124
Conformity Assessment Route(s):	Annex IX of the MDR, assessment of Full Quality Assurance System and Technical Documentation

Artivion, Inc., herewith declares under sole responsibility that the above-mentioned medical devices are in accordance with all applicable requirements of the Medical Device Regulation (EU)

2017/745. In addition, the BioGlue Surgical Adhesive implant material meets the requirements of EU Regulation 722/2012.

This declaration was issued based on the Full Quality Assurance Certificate No. 51523-60-00 issued 19-Dec-2022 and EC Certificate No. 51523-61-A0 issued 19-Dec-2022.

Standards applied to the medical device. (See Attachment #2)

Authorized Signatory:

DocuSigned by Drew Green
Drew Green | I approve this document
22-Dec-2022 | 4:02:15 PM EST
A52E56718B4A430FA51BC60A79362F48

22-Dec-2022

Drew Green
Vice President, Regulatory Affairs
Artivion, Inc.
Kennesaw, Georgia, USA

Date

Artivion, Inc.
1655 Roberts Blvd, NW, Kennesaw, GA 30144

ARTIVION
Formerly CryoLife | Jotec
artivion.com

Attachment 1

BioGlue® Surgical Adhesive
Declaration of Conformity Schedule of Product Codes
Revision Date: December 22, 2022

Product Code	Description of Product	Basic UDI-DI	GMDN Code	CND Code
BG3502-5-G	5 Pack, BioGlue Surgical Adhesive Syringes, 2 mL	87723400BG35007W	47784[1]	H90010101[2]
BG3510-5-G	5 Pack, BioGlue Surgical Adhesive Syringes, 10 mL			
BG3515-5-G	5 Pack, BioGlue Surgical Adhesive Syringes, 5 mL			

[1] GMDN 47784, Surgical internal adhesive/sealant, animal-derived: A bioabsorbable substance containing animal-derived material [e.g., bovine serum albumin (BSA)/cross-linking agent] intended to be used for internal surgical applications to bond or seal cut, incised, or resected body tissues (e.g., for vascular anastomosis) typically as an adjunct to standard methods of closure, to seal leaks, and might in addition be intended to achieve haemostasis through tissue sealing. Disposable mixing devices/applicators may be included for preparation and application to anatomical sites. After application, this device cannot be reused.
[2] CND H90010101, Tissue Glues, Biological

Artivion, Inc.
1655 Roberts Blvd, NW, Kennesaw, GA 30144

Attachment 2

Standards Applied

Standard	Title
EN ISO 13485:2016	Medical devices - Quality management system requirements for regulatory purposes
ISO 14971:2019	Medical devices – Application of risk management to medical devices
EN ISO 22442-1:2020	Medical devices utilizing animal tissues and their derivatives — Part 1: Application of risk management
EN ISO 22442-2:2020	Medical devices utilizing animal tissues and their derivatives — Part 2: Controls on sourcing, collection and handling
EN ISO 22442-3:2007	Medical devices utilizing animal tissues and their derivatives — Part 3: Validation of the elimination and/or inactivation of viruses and transmissible spongiform encephalopathy (TSE) agents
MEDDEV 2.7.1, Rev 4	Guidelines on Medical Devices Clinical Evaluation: A Guide for Manufacturers and Notified Bodies
MEDDEV 2.12.1, Rev 8	Guidelines on a Medical Devices Vigilance System
MEDDEV 2.12.2, Rev 2	Guidelines on Post Market Clinical Follow-Up
ISO 14155:2011	Clinical investigation of medical devices for human subjects — Good clinical practice
ISO 10993-1:2018	Biological Evaluation of Medical devices – Part 1: Evaluation and testing within a risk management process
ISO 10993-2:2006	Biological Evaluation of Medical devices – Part 2: Animal welfare requirements
ISO 10993-3:2014	Biological Evaluation of Medical devices – Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity
ISO 10993-4:2017	Biological Evaluation of Medical devices – Part 4: Selection of tests for interactions with blood
ISO 10993-5:2009	Biological Evaluation of Medical devices – Part 5: Tests for in vitro cytotoxicity
ISO 10993-6:2016	Biological Evaluation of Medical devices – Part 6: Tests for local effects after implantation
ISO 10993-9:2019	Biological Evaluation of Medical devices – Part 9: Framework for identification and quantification of potential degradation products
ISO 10993-10:2010	Biological Evaluation of Medical devices – Part 10: Tests for irritation and skin sensitization
ISO 10993-11:2017	Biological Evaluation of Medical devices – Part 11: Tests for systemic toxicity
ISO 10993-17:2002	Biological Evaluation of Medical devices – Part 17: Methods for the establishment of allowable limits for leachable substances
ISO/TS 10993-20:2006	Biological Evaluation of Medical devices – Part 20: Principles and methods for immunotoxicology testing of

Artivion, Inc.
1655 Roberts Blvd, NW, Kennesaw, GA 30144

Standard	Title
	medical devices
ISO 11137-1:2006/AMD 2:2018	Sterilization of health care products - Radiation - Part 1: Requirements for development, validation and routine control of a sterilization process for medical devices
ISO 11137-2:2013	Sterilization of health care products – Radiation – Part 2: Establishing the sterilization dose
ISO 11737-1:2018	Sterilization of health care products- Microbiological Methods - Part 1: Determination of a population of microorganisms on products
ANSI/AAMI/ISO 11737-2:2019	Sterilization of medical devices - Microbiological methods - Part 2: Tests of sterility performed in the definition, validation and maintenance of a sterilization process
ISO 14644-1:2015	Cleanrooms and associated controlled environments -- Part 1: Classification of air cleanliness by particle concentration
ISO 14644-2:2015	Cleanrooms and associated controlled environments — Part 2: Monitoring to provide evidence of cleanroom performance related to air cleanliness by particle concentration
GHTF/SG3/N99-10:2004	Quality Management Systems - Process Validation Guidance
BS EN ISO 14630:2012	Non-active surgical implants – General requirements
EN 1041:2008+A1:2013	Information supplied by the manufacturer of medical devices. AMD: October 31, 2013
ISO 15223-1:2021	Medical devices- Symbols to be used with medical device labels, labelling and information to be supplied, Part 1: General requirements
ASTM F2503-20	Standard practice for marking Medical Devices and other items for Safety in the Magnetic Field
ISO 11607-1:2019	Packaging for terminally sterilized medical devices—Part 1: Requirements for materials, sterile barrier systems and packaging system
ISO 11607-2:2019	Packaging for terminally sterilized medical devices -- Part 2: Validation requirements for forming, sealing and assembly processes
ASTM F88/F88M-15	Standard Test Method for Seal Strength of Flexible Barrier Materials
ASTM D4169-16	Standard Practice for Performance Testing of Shipping Containers and Systems
ASTM F2096-11	Standard Test Method for Detecting Gross Leaks in Medical Packaging by Internal Pressurization (Bubble Test)
ANSI/AAMI ST72:2019	Bacterial Endotoxins- Test Methods, Routine Monitoring, and Alternatives to Batch Testing
ASTM F2052-15	Standard Test Method for Measurement of Magnetically Induced Displacement Force on Medical Devices in the Magnetic Resonance Environment

Artivion, Inc.
1655 Roberts Blvd, NW, Kennesaw, GA 30144

EU Certificate

for the assessment of the technical documentation

according to Medical Device Regulation (EU) 2017/745 Annex IX Chapter II

As a Notified Body of the European Union, DEKRA Certification GmbH certifies, that the manufacturer

Artivion Inc.

Single Registration Number (SRN): US-MF-000015763
1655 Roberts Boulevard NW, 30144 Kennesaw, USA

Name, address of the authorized representative:
Jotec GmbH Lotzenäcker 23, 72379 Hechingen, Germany

that the technical documentation of the product(s) described in the annex complies with the provisions of the Medical Device Directive (EU) 2017/745. The certificate is based on the results of the assessment of the technical documentation according to the Medical Devices Regulation (EU) 2017/745 Annex IX Chapter II, which are recorded in the report referred to in the annex.

Product: BioGlue® Surgical Adhesive

EU Certificate no.: 51523-61-A0

Certificate valid from: 2022-12-19
Certificate valid to: 2027-12-18

DEKRA Certification GmbH Stuttgart, Handwerkstraße 15 D-70565 Stuttgart

Benannt durch/Designated by
Zentralstelle der Länder für Gesundheitsschutz bei Arzneimitteln und Medizinprodukten
www.zlg.de
BS-MDR-092

Natascha Jezyschek
DEKRA Certification GmbH, Stuttgart, 2022-12-19
Notified Body ID number: 0124

Annex to the EU Certificate no. 51523-61-A0

valid from 2022-12-19 to 2027-12-18

Revision status of the annex: 0 dated 2022-12-19

Report Number: 51523-TD1-04

Product: BioGlue® Surgical Adhesive

Basis-UDI-DI: 87723400BG35007W

Risk Classification: Class III

Intended Use:

BioGlue Surgical Adhesive is indicated for use as an adjunct to standard methods of surgical repair (such as sutures, staples, and/or patches) to adhere, seal, and/or reinforce soft tissue. Indicated soft tissues are cardiac, vascular, pulmonary, and dural.

Technical Data:

5 Pack, BioGlue Surgical Adhesive Syringes, 2 mL	BG3502-5-G
5 Pack, BioGlue Surgical Adhesive Syringes, 10 mL	BG3510-5-G
5 Pack, BioGlue Surgical Adhesive Syringes, 5 mL	BG3515-5-G

Remark: For the placing on the market of the product(s) referred to above, an additional EU certificate for the assessment of the quality management system in accordance with Annex IX Chapter I is required.

Natascha Jezyschek
DEKRA Certification GmbH, Stuttgart, 2022-12-19
Notified Body ID-number: 0124