Medtronic

Avalus™ Bioprosthesis

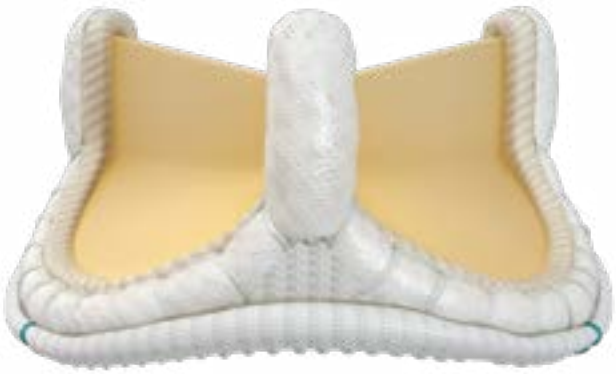
Designed for life.

Intentionally designed for durability and performance – from the frame materials and tissue treatment to leaflet manufacturing – the Avalus valve is made to last.

The Avalus valve delivers the durability and valve performance you expect – and that your patients deserve.

Built circular to stay circular

AOA™ tissue treatment



Designed for 100% coaptation and 0% doubt

Designed for future valve-in-valve (ViV)

Not all valves maintain circularity

A study analyzing 152 MDCT scans of stented surgical aortic valves showed none or trivial deformation in 44% of patients, mild deformation in 39% of patients, and noncircularity in

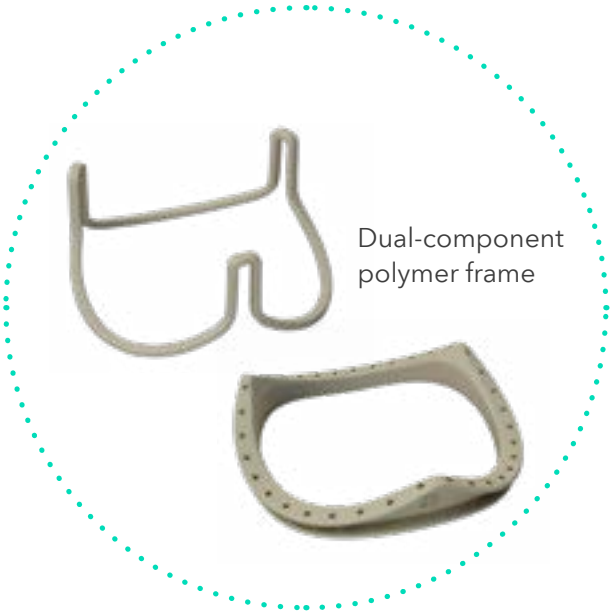
17% **of cases.**[1]

Built circular to stay circular

Circularity is crucial, but not all aortic valves stay circular. Noncircular or deformed surgical valves can have decreased durability and poor blood flow.[1-5] The nondeformable polymer base of the Avalus surgical aortic valve is designed to[1,2]:

- Enable efficient blood flow
- Allow regular leaflet motion
- Increase valve durability
- Help facilitate future ViV procedures

Surgical valve replacement risks may include infection, surgical complications, stroke, endocarditis, and death.



The Avalus valve utilizes a nondeformable polymer (PEEK) base which allows the valve to maintain circularity during and post-implantation, which can be critical for long-term hemodynamic performance and stability.[2-5]

[1] Faure ME, Suchá D, Schwartz FR, et al. Surgically implanted aortic valve bioprostheses deform after implantation: insights from computed tomography. *Eur Radiol*. May 2020;30(5):2651-2657.

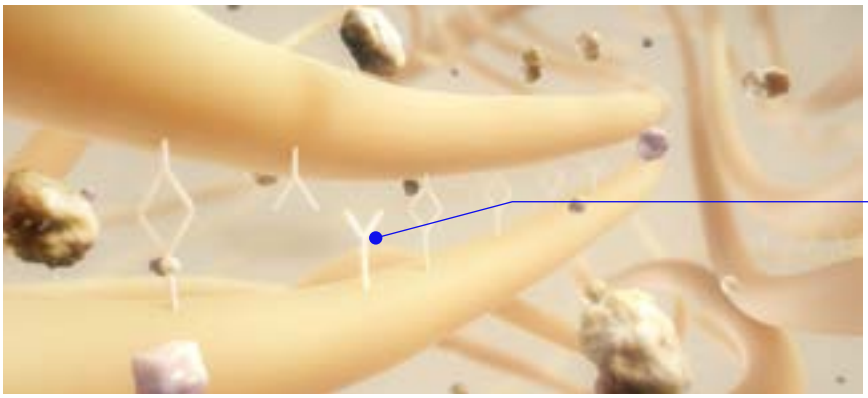
[2] Gunning PS, Saikrishnan N, Yoganathan AP, McNamara LM. Total ellipse of the heart valve: the impact of eccentric stent distortion on the regional dynamic deformation of pericardial tissue leaflets of a transcatheter aortic valve replacement. *J R Soc Interface*. December 6, 2015;12(113):20150737.

[3] Flameng W, Herregods M-C, Vercalsteren M, Herijgers P, Bogaerts K, Meuris B. Prosthesis-patient mismatch predicts structural valve degeneration in bioprosthetic heart valves. *Circulation*. May 18, 2010;121(19):2123-2129.

[4] Sritharan D, Fathi P, Weaver JD, Retta SM, Wu C, Duraiswamy N. Impact of clinically relevant elliptical deformations on the damage patterns of sagging and stretched leaflets in a bioprosthetic heart valve. *Cardiovasc Eng Technol*. September 2018;9(3):351-364.

[5] Ruzicka DJ, Hettich I, Hutter A, et al. The complete supraannular concept. *Circulation*. 2009;120[suppl 1]:S139-S145.

AOA tissue treatment

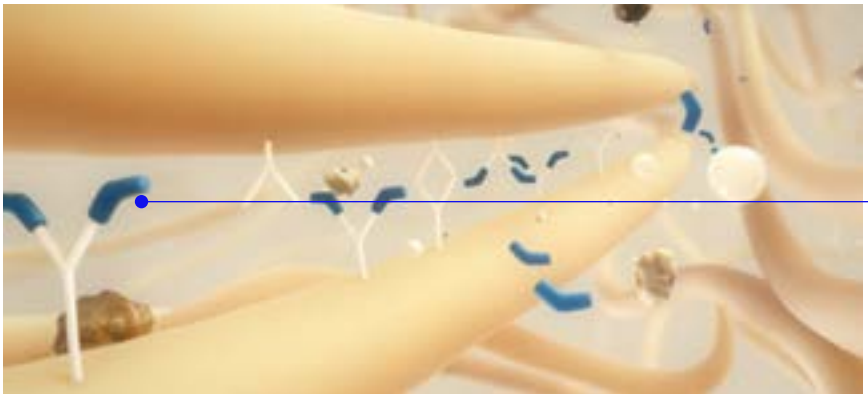


After tissue fixation[1-3]

Free aldehydes present

AOA treatment[1-3]

AOA covalently bonds with free aldehydes; lipids are washed away



After treatment[1-3]

Large AOA molecule slows diffusion of calcium into tissue matrix

30+

years of clinical use

Valves treated with AOA* have been implanted in 500,000+ patients. AOA treatment is utilized across multiple products, such as Mosaic™ aortic and mitral valves, Freestyle™ aortic valve, and Evolut™ transcatheter platform.

*The benefits of AOA tissue treatment have been demonstrated through animal testing. No direct clinical evaluation of the benefits of AOA treatment in humans has been conducted.

[1] Gott JP, Pan-Chih L, Dorsey, JL, et al. Calcification of porcine valves: A successful new method of antimineralization. *Ann Thorac Surg.* 1992;53:207-216.

[2] Girardot MN, Girardot JM, Schoen FJ. Development of the AOA process as antimineralization treatment for bioprosthetic heart valves. *Trans. Soc. Biomat.* 1993;16:266.

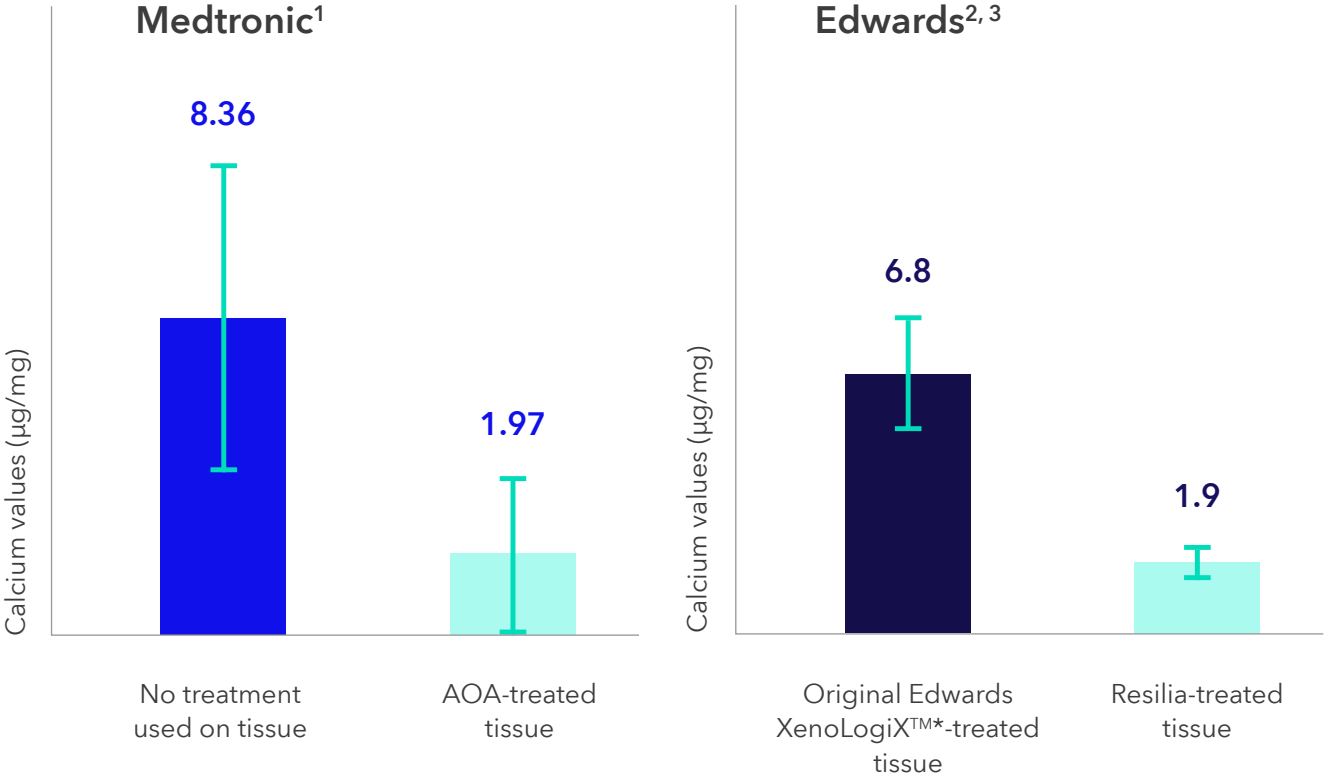
[3] Girardot MN, Torrianni M, Girardot FJ. Effect of AOA on glutaraldehyde-fixed bioprosthetic heart valve cusps and walls: Binding and calcification studies. *Int J Artif Organs.* 1994;17:127-133.

Calcium reduction

Medtronic and Edwards Lifesciences each studied anti-calcification treatments in the mitral position of juvenile sheep. In both respective studies, AOA and Edwards Resilia™* treatments demonstrated similar significant reduction in calcium compared to the control group.

Did you know?

Subsequent storage in glutaraldehyde allows any remaining free aldehydes to crosslink.[4, 5]



These tests may not be indicative of clinical performance and are for illustrative purposes only. The charts are not intended to be a comparison of the two devices as there is no head-to-head preclinical animal clinical study but rather are intended to illustrate the results of two similar animal studies. Multiple factors contribute to animal study outcomes and need to be considered in making any assessments across different studies.

[1] Weber PA, Jouan J, Matsunaga A, et al. Evidence of mitigated calcification of the Mosaic versus Hancock Standard valve xenograft in the mitral position of young sheep. *J Thorac Cardiovasc Surg*. November 2006;132(5):1137-1143.

[2] Flameng W, Hermans H, Verbeken E, Meuris B. A randomized assessment of an advanced tissue preservation technology in the juvenile sheep model. *J Thorac Cardiovasc Surg*. January 2015;149(1):340-345.

[3] Puskas JD, Bavaria JE, Svensson LG, et al. The COMMENCE trial: 2-year outcomes with an aortic bioprosthesis with RESILIA tissue. *Eur J Cardiothorac Surg*. September 1, 2017;52(3):432-439.

[4] Giradot MN, Giradot JM, Torriani M. Alpha-aminiooleic acid (AOA) effectiveness on glutaraldehyde-fixed heart valves: Shelf-life studies. In, New Horizons and the Future of Heart Valve Bioprostheses, First edition.

[5] Zilla P, Weissenstein C, Human P, et al. High glutaraldehyde concentrations mitigate bioprosthetic root calcification in the sheep model. *Ann Thorac Surg*. 2000;70:2091-2095.

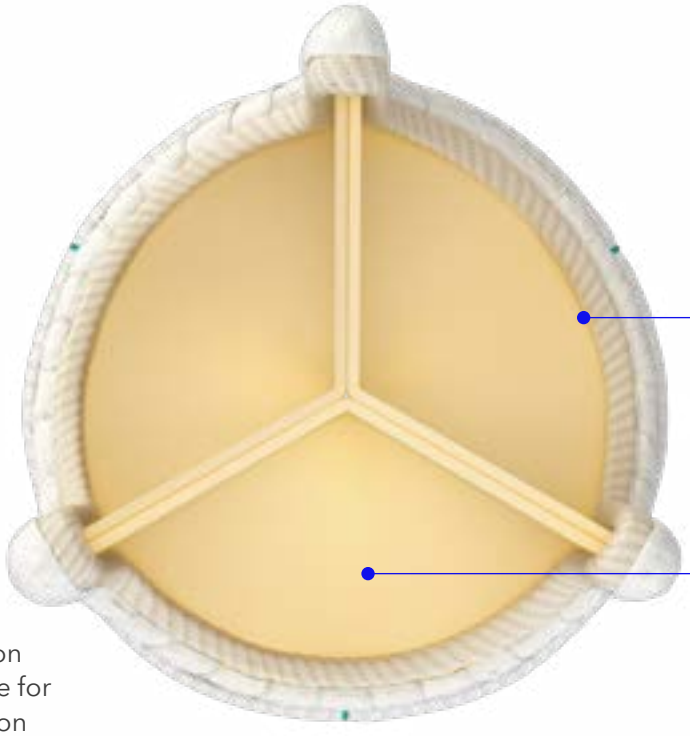
Designed for 100% coaptation and 0% doubt

The Avalus valve features a dual component, nondeformable base, and flexible stent posts designed for:

- Excellent leaflet coaptation[1,2]
- Coapts smoothly and fully to effectively reduce central jet of blood flow[1,2]
- Supra-annular placement

Design highlights

Avalus valve was designed to maximize the advantages of an internally mounted valve while reducing its key disadvantage, which is greater central regurgitation.



Laser-cut holes in leaflets align with corresponding holes in stent for consistent valve assembly

Stent post deflection specific to each size for maximum coaptation

Leaflet tissue thickness specific to each size

[1] Klautz RJM, Rao V, Reardon MJ, et al. Hemodynamic function of contemporary surgical aortic valves 1 year postimplant. Paper presented at: 37th Annual Meeting of the European Association for Cardio-Thoracic Surgery; October 4–7, 2023; Vienna, Austria.

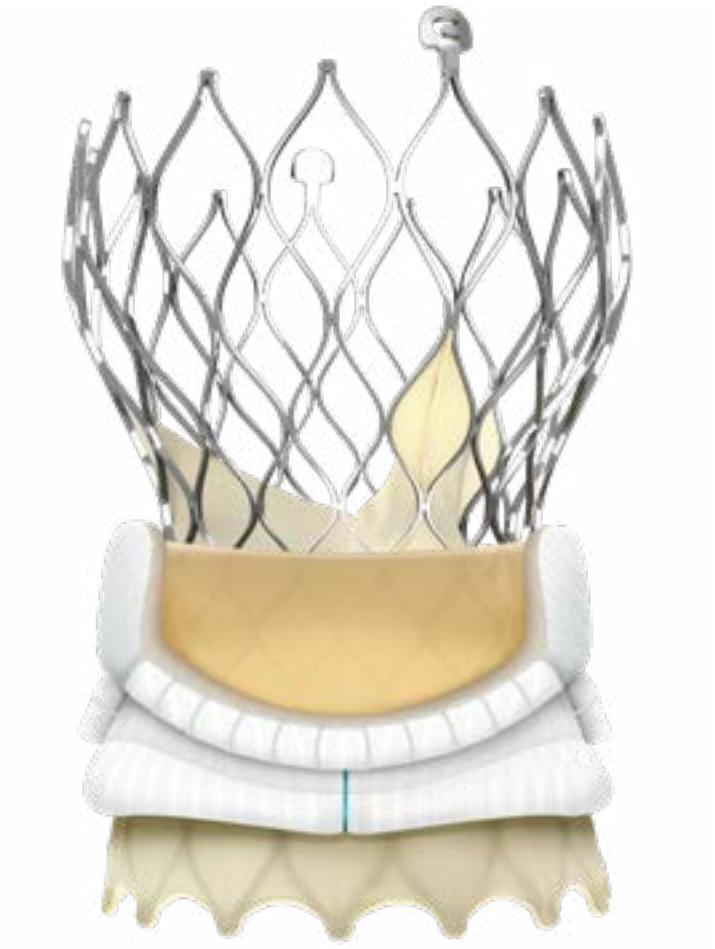
[2] Vriesendorp MD, de Lind van Wijngaarden RAF, Rao V, et al. An in vitro comparison of internally versus externally mounted leaflets in surgical aortic bioprostheses. *Interactive CardioVascular and Thoracic Surgery.* March 1, 2020;30(3):417-423.

Facilitates future ViV patient care

- The polymer frame does not contain any metal to reduce risk of metal-on-metal corrosion with transcatheter stent materials.
- The base frame is made from PEEK and impregnated with barium sulfate to help provide radiopacity, which facilitates ViV procedures.
- Interior-mounted leaflets reduce the risk of coronary obstruction in ViV procedures.
- MRI-safe in all MR environments without conditions.

Did you know?

Both the Avalus and transcatheter Evolut™ valves are designed for the valve leaflets to be supra-annular.

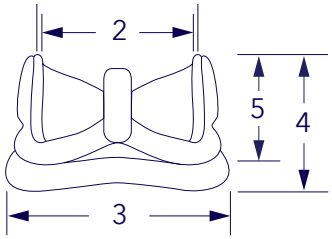


Ordering information

Item number	Valve size	Stent diameter (TAD)	Internal orifice diameter†		External sewing ring diameter	Valve profile height	Aortic protrusion
		(1)	(2)	(2a)	(3)	(4)	(5)
40019	19 mm	19 mm	17.5 mm	18 mm	27.0 mm	13.0 mm	11.0 mm
40021	21 mm	21 mm	19.5 mm	20 mm	29.0 mm	14.0 mm	12.0 mm
40023	23 mm	23 mm	21.5 mm	22 mm	31.0 mm	15.0 mm	13.0 mm
40025	25 mm	25 mm	23.5 mm	24 mm	33.0 mm	16.0 mm	14.0 mm
40027	27 mm	27 mm	25.5 mm	26 mm	36.0 mm	17.0 mm	15.0 mm
40029	29 mm	29 mm	27.5 mm	28 mm	37.0 mm	18.0 mm	16.0 mm

TAD: Tissue Annulus Diameter

†Measurement shows stent frame including tissue (2) and stent frame excluding tissue (2a).



Accessories

Item number	Description
7420	Valve handle
7400S	Avalus sizer
T7400	Avalus tray
7779	Jar wrench

Indications, safety, and warnings

If you are located in the United States, please refer to the brief statement(s) below to review applicable indications, safety, and warning information. See the device manual for a full list of information regarding the instructions for use, the implant procedure, indications, contraindications, warnings, precautions, and potential complications/adverse events. For further information, please call Medtronic at 1.763.514.4000 and/or consult the Medtronic website at **medtronic.com**.

If you are located outside the United States, see the device manual for a full list of information regarding instructions for use, the implant procedure, indications, contraindications, warnings, precautions, and potential adverse events. For further information, contact your local Medtronic representative and/or consult the Medtronic website at **medtronic.com** and select your appropriate country/region.

For applicable products, consult instructions for use on **manuals.medtronic.com**. Manuals can be viewed using a current version of any major internet browser. For best results, use Adobe Acrobat® Reader with the browser.

Avalus™ Bioprosthesis

Indications
The Avalus bioprosthesis is indicated for the replacement of diseased, damaged, or malfunctioning native or prosthetic aortic valves.

Contraindications
None known.

Warnings/Precautions/Adverse Events
Only physicians who have received proper training in valve replacement should use this device. Accelerated structural deterioration due to calcific degeneration of bioprosthesis may occur in: children, adolescents, young adults, and patients with altered calcium metabolism (e.g., chronic renal failure, or hyperparathyroidism). Adverse events can include: angina, cardiac dysrhythmias, endocarditis, heart failure, hemolysis, hemolytic anemia, hemorrhage, infection other than endocarditis, transvalvular or paravalvular leak, myocardial infarction, nonstructural valve dysfunction (leaflet entrapment/impingement, obstructive pannus ingrowth, suture dehiscence, inappropriate sizing or positioning, or other), pericardial effusion or tamponade, prosthesis regurgitation, prosthesis stenosis, prosthesis thrombosis, stroke, structural valve deterioration (calcification, leaflet tear or perforation, or other), thromboembolism, tissue dehiscence, and transient ischemic attack. These complications could lead to reoperation, explant of the bioprosthesis, permanent disability, or death.

Caution
Federal law (USA) restricts these devices to sale by or on the order of a physician.

Evolut™ TAVR System

Indications
The Medtronic Evolut™ PRO+, Evolut™ FX, and Evolut™ FX+ Systems are indicated for relief of aortic stenosis in patients with symptomatic heart disease due to severe native calcific aortic stenosis who are judged by a heart team, including a cardiac surgeon, to be appropriate for the transcatheter heart valve replacement therapy.

The Medtronic Evolut PRO+, Evolut FX, and Evolut FX+ Systems are indicated for use in patients with symptomatic heart disease due to failure (stenosed, insufficient, or combined) of a surgical bioprosthetic aortic valve who are judged by a heart team, including a cardiac surgeon, to be at high or greater risk for open surgical therapy (e.g., STS predicted risk of operative mortality score ≥ 8% or at a ≥ 15% risk of mortality at 30 days).

Contraindications
The Medtronic Evolut PRO+, Evolut FX, and Evolut FX+ Systems are contraindicated in patients who cannot tolerate Nitinol (titanium or nickel), gold (for Evolut FX and Evolut FX+ Systems alone), an anticoagulation/antiplatelet regimen, or who have active bacterial endocarditis or other active infections.

Warnings
General Implantation of the Evolut PRO+, Evolut FX, and Evolut FX+ Systems should be performed only by physicians who have received Medtronic Evolut PRO+, Evolut FX, or Evolut FX+ training. This procedure should only be performed where emergency aortic valve surgery can be performed promptly. Mechanical failure of the delivery catheter system and/or accessories may result in patient complications. Transcatheter aortic valve (bioprosthesis) Accelerated deterioration due to calcific degeneration of the bioprostheses may occur in: children, adolescents, or young adults; patients with altered calcium metabolism (e.g., chronic renal failure or hyperthyroidism).

Precautions
General Clinical long-term durability has not been established for the bioprosthesis. Evaluate bioprosthesis performance as needed during patient follow-up. The safety and effectiveness of the Evolut PRO+, Evolut FX, and Evolut FX+ Systems have not been evaluated in the pediatric population. The safety and effectiveness of the bioprostheses for aortic valve replacement have not been evaluated in the following patient populations:

Patients who do not meet the criteria for symptomatic severe native aortic stenosis as defined: (1) symptomatic severe high-gradient aortic stenosis – aortic valve area ≤ 1.0 cm2 or aortic valve area index ≤ 0.6 cm2/m2, a mean aortic valve gradient ≥ 40 mm Hg, or a peak aortic-jet velocity ≥ 4.0 m/s; (2) symptomatic severe low-flow, low-gradient aortic stenosis – aortic valve area ≤ 1.0 cm2 or aortic valve area index ≤ 0.6 cm2/m2, a mean aortic valve gradient < 40 mm Hg, and a peak aortic-jet velocity < 4.0 m/s; with untreated, clinically significant coronary artery disease requiring revascularization; with a preexisting prosthetic heart valve with a rigid support structure in either the mitral or pulmonic position if either the preexisting prosthetic heart valve could affect the implantation or function of the bioprosthesis or the implantation of the bioprosthesis could affect the function of the preexisting prosthetic heart valve; patients with liver failure (Child-Pugh Class C); with cardiogenic shock manifested by low cardiac output, vasopressor dependence, or mechanical hemodynamic support; patients who are pregnant or breastfeeding. The safety and effectiveness of an Evolut PRO+, Evolut FX, or Evolut FX+ bioprosthesis implanted within a failed preexisting transcatheter bioprosthesis have not been demonstrated. Implanting an Evolut PRO+, Evolut FX, or Evolut FX+ bioprosthesis in a degenerated surgical bioprosthetic valve (transcatheter aortic valve in surgical aortic valve [TAV-in-SAV]) should be avoided in the following conditions: The degenerated surgical bioprosthetic valve presents with: a significant concomitant paravalvular leak (between the prosthesis and the native annulus), is not securely fixed in the native annulus, or is not structurally intact (e.g., wire form frame fracture); partially detached leaflet that in the aortic position may obstruct a coronary ostium; stent frame with a manufacturer-labeled inner diameter < 17 mm. The safety and effectiveness of the bioprostheses for aortic valve replacement have not been evaluated in patient populations presenting with the following: Blood dyscrasias as defined as leukopenia (WBC < 1,000 cells/mm3), thrombocytopenia (platelet count < 50,000 cells/mm3), history of bleeding diathesis or coagulopathy, or hypercoagulable states; congenital unicuspid valve; mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation [3-4+]); moderate to severe (3-4+) or severe (4+) mitral or severe (4+) tricuspid regurgitation; hypertrophic obstructive cardiomyopathy; new or untreated echocardiographic evidence of intracardiac mass, thrombus, or vegetation; native aortic annulus size < 18 mm or > 30 mm per the baseline diagnostic imaging or surgical bioprosthetic aortic annulus size < 17 mm or > 30 mm; transarterial access unable to accommodate an 18 Fr introducer sheath or the 14 Fr equivalent Evolut PRO+ inline sheath when using model D-EVPROP2329US or Evolut FX Delivery Catheter System with inline sheath when using model D-EVOLUTFX-2329 or transarterial access unable to accommodate a 22 Fr introducer sheath or the 18 Fr equivalent Evolut PRO+ inline sheath when using model D-EVPROP34US or Evolut FX Delivery Catheter System with inline sheath when using model D-EVOLUTFX-34; prohibitive left ventricular outflow tract calcification; sinus of Valsalva anatomy that would prevent adequate coronary perfusion; significant aortopathy requiring ascending aortic replacement; moderate to severe mitral stenosis; severe ventricular dysfunction with left ventricular ejection fraction (LVEF) < 20%; symptomatic carotid or vertebral artery disease; and severe basal septal hypertrophy with an outflow gradient.

Before Use Exposure to glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to the vapors. Damage may result from forceful handling of the catheter. Prevent kinking of the catheter when removing it from the packaging. The bioprosthesis size must be appropriate to fit the patient's anatomy. Proper sizing of the devices is the responsibility of the physician. Refer to the Instructions for Use for available sizes. Failure to implant a device within the sizing matrix could lead to adverse effects such as those listed below. Patients must present with transarterial access vessel diameters of ≥ 5 mm when using models D-EVPROP2329US/D-EVOLUTFX-2329 or ≥ 6 mm when using models D-EVPROP34US/D-EVOLUTFX-34, or patients must present with an ascending aortic (direct aortic) access site ≥ 60 mm from the basal plane for both systems. Implantation of the bioprosthesis should be avoided in patients with aortic root angulation (angle between plane of aortic valve annulus and horizontal plane/vertebrae) of > 30° for right subclavian/axillary access or > 70° for femoral and left subclavian/axillary access. For subclavian access, patients with a patent left internal mammary artery (LIMA) graft must present with access vessel diameters that are either ≥ 5.5 mm when using models D-EVPROP2329US/D-EVOLUTFX-2329 or ≥ 6.5 mm when using models D-EVPROP34US/D-EVOLUTFX-34. Use caution when using the subclavian/axillary approach in patients with a patent LIMA graft or patent RIMA graft. For direct aortic access, ensure the access site and trajectory are free of patent RIMA or a preexisting patent RIMA graft. For transfemoral access, use caution in patients who present with multiplanar curvature of the aorta, acute angulation of the aortic arch, an ascending aortic aneurysm, or severe calcification in the aorta and/or vasculature. If ≥ 2 of these factors are present, consider an alternative access route to prevent vascular complications. Limited clinical data are available for transcatheter aortic valve replacement in patients with a congenital bicuspid aortic valve who are deemed to be at low surgical risk. Anatomical characteristics should be considered when using the valve in this population. In addition, patient age should be considered as long-term durability of the valve has not been established.

During Use If a misload is detected during fluoroscopic inspection, do not attempt to reload the bioprosthesis. Discard the entire system. Inflow crown overlap that has not ended before the 4th node within the capsule increases the risk of an infold upon deployment in constrained anatomies, particularly with moderate-severe levels of calcification and/or bicuspid condition. Do not attempt to direct load the valve. After the procedure, administer appropriate antibiotic prophylaxis as needed for patients at risk for prosthetic valve infection and endocarditis. After the procedure, administer anticoagulation and/or antiplatelet therapy per physician/clinical judgment. Excessive contrast media may cause renal failure. Prior to the procedure, measure the patient's creatinine level. During the procedure, monitor contrast media usage. Conduct the procedure under fluoroscopy. Fluoroscopic procedures are associated with the risk of radiation damage to the skin, which may be painful, disfiguring, and long-term. The safety and efficacy of an Evolut PRO+, Evolut FX, or Evolut FX+ bioprosthesis implanted within a transcatheter bioprosthesis have not been demonstrated.

Potential adverse events
Potential risks associated with the implantation of the Evolut PRO+, Evolut FX, or Evolut FX+ transcatheter aortic valve may include, but are not limited to, the following: • death • myocardial infarction, cardiac arrest, cardiogenic shock, or cardiac tamponade • coronary occlusion, obstruction, or vessel spasm (including acute coronary closure) • cardiovascular injury (including rupture, perforation, tissue erosion, or dissection of vessels, ascending aorta trauma, ventricle, myocardium, or valvular structures that may require intervention) • emergent surgical or transcatheter intervention (e.g., coronary artery bypass, heart valve replacement, valve explant, percutaneous coronary intervention [PCI], balloon valvuloplasty) • prosthetic valve dysfunction (regurgitation or stenosis) due to fracture; bending (out-of-round configuration) of the valve frame; underexpansion of the valve frame; calcification; pannus; leaflet wear, tear, prolapse, or retraction; poor valve coaptation; suture breaks or disruption; leaks; mal-sizing (prosthesis-patient mismatch); malposition (either too high or too low)/malplacement – prosthetic valve migration/embolization • prosthetic valve endocarditis • prosthetic valve thrombosis • delivery catheter system malfunction resulting in the need for additional recrossing of the aortic valve and prolonged procedural time • delivery catheter system component migration/embolization • stroke (ischemic or hemorrhagic), transient ischemic attack (TIA), or other neurological deficits • individual organ (e.g., cardiac, respiratory, renal [including acute kidney failure]) or multi-organ insufficiency or failure • major or minor bleeding that may require transfusion or intervention (including life-threatening or disabling bleeding) • vascular access-related complications (e.g., dissection, perforation, pain, bleeding, hematoma, pseudoaneurysm, irreversible nerve injury, compartment syndrome, arteriovenous fistula, or stenosis) • mitral valve regurgitation or injury • conduction system disturbances (e.g., atrioventricular node block, left bundle-branch block, asystole), which may require a permanent pacemaker • infection (including septicemia) • hypotension or hypertension • hemolysis • peripheral ischemia • General surgical risks applicable to transcatheter aortic valve implantation: • bowel ischemia • abnormal lab values (including electrolyte imbalance) • allergic reaction to antiplatelet agents, contrast medium, or anesthesia • exposure to radiation through fluoroscopy and angiography • permanent disability.

Please reference the Evolut PRO+, Evolut FX, and Evolut FX+ Instructions for Use for more information regarding indications, warnings, precautions, and potential adverse events.

Caution: Federal Law (USA) restricts these devices to the sale by or on the order of a physician.

The commercial name of the Evolut™ PRO+ device is Medtronic Evolut™ PRO+ System, the commercial name of the Evolut™ FX device is Medtronic Evolut™ FX System, and the commercial name of the Evolut™ FX+ device is Medtronic Evolut™ FX+ System.

Freestyle™ Aortic Root Bioprosthesis

Indications
For the replacement of malfunctioning native or prosthetic aortic valves with the option of aortic root replacement.

Contraindications
None known.

Warnings/Precautions/Adverse Events
Accelerated deterioration due to calcific degeneration of bioprosthesis may occur in: children, adolescents, young adults, and patients with altered calcium metabolism (e.g., chronic renal failure, hyperparathyroidism). Adverse events can include: cardiac dysrhythmias, death, endocarditis, heart failure, hemolysis, hemorrhage, transvalvular or paravalvular leak, nonstructural dysfunction, structural deterioration, thromboembolism, valve thrombosis, or intracuspal hematoma.

Caution
Federal law (USA) restricts these devices to sale by or on the order of a physician.

Mosaic™ Bioprosthesis

Indications
For the replacement of malfunctioning native or prosthetic aortic and/or mitral heart valves.

Contraindications
None known.

Warnings/Precautions/Adverse Events
Accelerated deterioration due to calcific degeneration of bioprosthesis may occur in: children, adolescents, young adults, and patients with altered calcium metabolism (e.g., chronic renal failure, hyperparathyroidism). Adverse events can include: angina, cardiac arrhythmia, cardiac dysrhythmias, death, endocarditis, infection other than endocarditis, heart failure, hemolysis, hemolytic anemia, hemorrhage, transvalvular or paravalvular leak, myocardial infarction, nonstructural dysfunction, stroke, structural deterioration, thromboembolism, or valve thrombosis.

Caution
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