Edwards Lifesciences Heart Valve Leadership

The Edwards SAPIEN 3 transcatheter heart valve builds on Edwards Lifesciences' more than 50 years of continuous refinement in heart valve technologies, and successful collaboration with clinicians to develop leading medical devices.

Tissue and Mechanical Valves
There are two general types of valves used for aortic valve replacement: mechanical and tissue. Some reports suggest that the mechanical valves available today have practically unlimited durability, but patients must take blood thinning medication (anticoagulation therapy) to prevent the formation of blood clots, which requires regular monitoring. As severe bleeding is a risk while taking blood thinners, patients must exercise caution when participating in certain activities and avoid situations that increase the risk of injury. Edwards is the worldwide leader in tissue heart valves. Decades of clinical experience and peer-reviewed data on Edwards' proven surgical family of bovine pericardial tissue valves provide robust evidence of long-term durability and proven hemodynamics.

More than 50 Years of Experience in Surgical Valves
Edwards established its leadership in heart valve therapy first with the development of the Starr-Edwards mechanical valve and later with the world's most widely implanted tissue valves, the PERIMOUNT family of valves. Decades of refinement through experience, scientifically rigorous studies and further collaboration with clinicians – including with those who performed the first successful TAVR on a human patient in April 2002 – led to the innovation of the Edwards SAPIEN platform of valves. The manufacturing processes used for the Edwards SAPIEN platform of valves are based on the processes used for the company's foundational surgical tissue valves.

Edwards' Next-Generation Transcatheter Valves
The SAPIEN 3 valve was approved by the U.S. Food and Drug Administration (FDA) in June 2015 as a therapy for patients with severe aortic stenosis who have been determined by a Heart Team to be at high or greater risk for open-heart surgery. In August 2016, the FDA approved the SAPIEN 3 valve for an expanded indication to include patients at intermediate risk for open-heart surgery, further extending Edwards' global leadership in transcatheter valve technology. To date, more than 150,000 patients have been treated with Edwards' transcatheter valves by multi-disciplinary Heart Teams worldwide.

CAUTION: Federal (United States) law restricts these devices to sale by or on the order of a physician. See instructions for use for full prescribing information, including indications, contraindications, warnings, precautions and adverse events.

This document was updated in October 2016.

Additional Information
To review all important risks for the SAPIEN 3 valve, please visit SAPIEN3.com.

More information about the TAVR procedure can be found at NewHeartValve.com.

Milestones in the History of Edwards Lifesciences

- **1958** Miles "Lowell" Edwards begins work to create a replacement heart. Mr. Edwards meets Dr. Albert Starr, who suggests developing an artificial heart valve. Less than two years later, the Starr-Edwards Silastic ball valve is successfully implanted to replace the mitral valve in a patient's heart.
- **1965** Prof. Alain Carpentier implants the first porcine tissue heart valve into a patient and partners with Edwards to develop tissue heart valves.
- **1976** The Carpentier-Edwards porcine valve becomes one of the first tissue valves available worldwide.
- **1981** Edwards introduces the Carpentier-Edwards PERIMOUNT bovine pericardial aortic valve.
- **1995** Henning Andersen receives European patent for transcatheter heart valve technology.
- **2002** Prof. Alain Cribier performs the first successful TAVR on a human patient.
- **2004** Edwards completes purchase of Percutaneous Valve Technologies (PVT), combining the transcatheter aortic valve replacement (TAVR) work of PVT with Edwards' own internal program underway.
- **2007** Edwards launches the SAPIEN transcatheter heart valve in Europe.
- **2010** Edwards launches the SAPIEN XT transcatheter heart valve in Europe.
- **2011** Edwards introduces TAVR to U.S. patients with the launch of the SAPIEN valve.
- **2013** Edwards introduces TAVR to Japanese patients with the launch of the SAPIEN XT transcatheter heart valve.
- **2014** Edwards launches the SAPIEN 3 transcatheter valve in Europe.
- **2014** Edwards introduces transcatheter valve-in-valve technology to Europe for replacing bioprosthetic aortic and mitral valves using SAPIEN XT valve.
- **2014** Edwards launches the SAPIEN XT transcatheter heart valve in the U.S.
- **2015** Edwards launches the SAPIEN 3 transcatheter heart valve in the U.S.
- **2015** Edwards introduces transcatheter valve-in-valve technology to the U.S. for replacing bioprosthetic aortic valves using SAPIEN XT valve.
- **2016** Edwards receives FDA approval for the treatment of intermediate-risk patients with the SAPIEN 3 transcatheter valve.

IMPORTANT SAFETY INFORMATION

Edwards SAPIEN 3 Transcatheter Heart Valve with the Edwards Commander Delivery System

Indications: The Edwards SAPIEN 3 transcatheter heart valve, model 9600TFX, and accessories 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 at intermediate or greater risk for open surgical therapy (i.e., predicted risk of surgical mortality ≥ 3% at 30 days, based on the Society of Thoracic Surgeons (STS) risk score and other clinical co-morbidities unmeasured by the STS risk calculator).

Contraindications: The valve and delivery systems are contraindicated in patients who cannot tolerate an anticoagulation/antiplatelet regimen or who have active bacterial endocarditis or other active infections.

Warnings: Observation of the pacing lead throughout the procedure is essential to avoid the potential risk of pacing lead perforation. There may be an increased risk of stroke in transcatheter aortic valve replacement procedures, as compared to balloon aortic valvuloplasty or other standard treatments in high or greater risk patients. The devices are designed, intended, and distributed for single use only. **Do not resterilize or reuse the devices.** There are no data to support the sterility, nonpyrogenicity, and functionality of the devices after reprocessing. Incorrect sizing of the valve may lead to paravalvular leak, migration, embolization, and/or annular rupture. Accelerated deterioration of the valve may occur in patients with an altered calcium metabolism. Prior to delivery, the valve must remain hydrated at all times and cannot be exposed to solutions other than its shipping storage solution and sterile physiologic rinsing solution. Valve leaflets mishandled or damaged during any part of the procedure will require replacement of the valve. Caution should be exercised in implanting a valve in patients with clinically significant coronary artery disease. Patients with pre-existing mitral valve devices should be carefully assessed prior to implantation of the valve to ensure proper valve positioning and deployment. Do not mishandle the delivery system or use it if the packaging or any components are not sterile, have been opened or are damaged (e.g., kinked or stretched), or if the expiration date has elapsed. Use of excessive contrast media may lead to renal failure. Measure the patient's creatinine level prior to the procedure. Contrast media usage should be monitored. Patient injury could occur if the delivery system is not un-flexed prior to removal. Care should be exercised in patients with hypersensitivities to cobalt, nickel, chromium, molybdenum, titanium, manganese, silicon, and/or polymeric materials. The procedure should be conducted under fluoroscopic guidance. Some fluoroscopically guided procedures are associated with a risk of radiation injury to the skin. These injuries may be painful, disfiguring, and long-lasting. Valve recipients should be maintained on anticoagulant/antiplatelet therapy, except when contraindicated, as determined by their physician. This device has not been tested for use without anticoagulation.

Precautions: Long-term durability has not been established for the valve. Regular medical follow-up is advised to evaluate valve performance. Glutaraldehyde may cause irritation of the skin, eyes, nose, and throat. Avoid prolonged or repeated exposure to, or breathing of, the solution. To maintain proper valve leaflet coaptation, do not overinflate the deployment balloon. Appropriate antibiotic prophylaxis is recommended post-procedure in patients at risk for prosthetic valve infection and endocarditis. Safety, effectiveness, and durability have not been established for valve-in-valve procedures. Safety and effectiveness have not been established for patients with the following characteristics/comorbidities: non-calcified aortic annulus; severe ventricular dysfunction with ejection fraction < 20%; congenital unicuspid or congenital bicuspid aortic valve; mixed aortic valve disease (aortic stenosis and aortic regurgitation with predominant aortic regurgitation > 3+); pre-existing prosthetic heart valve or prosthetic ring in any position; severe mitral annular calcification (MAC), severe (> 3+) mitral insufficiency, or Gorlin syndrome; blood dyscrasias defined as leukopenia (WBC < 3000 cells/mL), acute anemia (Hb < 9 g/dL), thrombocytopenia (platelet count < 50,000 cells/mL), or history of bleeding diathesis or coagulopathy; hypertrophic cardiomyopathy with or without obstruction (HOCM); echocardiographic evidence of intracardiac mass, thrombus, or vegetation; a known hypersensitivity or contraindication to aspirin, heparin, ticlopidine (Ticlid), or clopidogrel (Plavix), or sensitivity to contrast media, which cannot be adequately premedicated; significant aortic disease, including abdominal aortic or thoracic aneurysm defined as maximal luminal diameter 5 cm or greater, marked tortuosity (hyperacute bend), aortic arch atheroma (especially if thick [> 5 mm], protruding, or ulcerated) or narrowing (especially with calcification and surface irregularities) of the abdominal or thoracic aorta, severe "unfolding" and tortuosity of the thoracic aorta; access characteristics that would preclude safe placement of 14F or 16F Edwards eSheath introducer set, such as severe obstructive calcification, severe tortuosity, or diameter less than 5.5 mm or 6 mm, respectively; or bulky calcified aortic valve leaflets in close proximity to coronary ostia.

Potential Adverse Events: Potential risks associated with the overall procedure including potential access complications associated with standard cardiac catheterization, balloon valvuloplasty, the potential risks of conscious sedation and/or general anesthesia, and the use of angiography: death; stroke/transient ischemic attack, clusters, or neurological deficit; paralysis; permanent disability; respiratory insufficiency or respiratory failure; hemorrhage requiring transfusion or intervention; cardiovascular injury including perforation or dissection of vessels, ventricle, myocardium, or valvular structures that may require intervention; pericardial effusion or cardiac tamponade; embolization including air, calcific valve material, or thrombus; infection including septicemia and endocarditis; heart failure; myocardial infarction; renal insufficiency or renal failure; conduction system defect which may require a permanent pacemaker; arrhythmia; retroperitoneal bleed; arteriovenous(AV) fistula or pseudoaneurysm; reoperation; ischemia or nerve injury; restenosis; pulmonary edema; pleural effusion; bleeding; anemia; abnormal lab values (including electrolyte imbalance); hypertension or hypotension; allergic reaction to anesthesia, contrast media, or device materials; hematoma; syncope; pain or changes at the access site; exercise intolerance or weakness; inflammation; angina; heart murmur; and fever. Additional potential risks associated with the use of the valve, delivery system, and/or accessories include: cardiac arrest; cardiogenic shock; emergency cardiac surgery; cardiac failure or low cardiac output; coronary flow obstruction/ transvalvular flow disturbance; device thrombosis requiring intervention; valve thrombosis; device embolization; device migration or malposition requiring intervention; valve deployment in unintended location; valve stenosis; structural valve deterioration (wear, fracture, calcification, leaflet tear/tearing from the stent posts, leaflet retraction, suture line disruption of components of a prosthetic valve, thickening, stenosis); device degeneration; paravalvular or transvalvular leak; valve regurgitation; hemolysis; device explants; nonstructural dysfunction; mechanical failure of delivery system and/or accessories; and non-emergent reoperation.

Edwards Crimper

Indications: The Edwards Crimper is indicated for use in preparing the Edwards SAPIEN 3 transcatheter heart valve for implantation.

Contraindications: There are no known contraindications.

Warnings: The devices are designed, intended, and distributed for single use only. Do not resterilize or reuse the devices. There is no data to support the sterility, nonpyrogenicity, and functionality of the devices after reprocessing.

Precautions: For special considerations associated with the use of the Edwards Crimper prior to transcatheter heart valve implantation, refer to the Edwards SAPIEN 3 transcatheter heart valve Instructions for Use.

Potential Adverse Events: There are no known potential adverse events associated with the Edwards Crimper.

Important Safety Information – Carpentier-Edwards PERIMOUNT Aortic Bioprostheses

Indications: For use in patients whose aortic valvular disease warrants replacement of their natural or previously placed prosthetic valve.

Contraindications: Do not use if surgeon believes it would be contrary to the patient's best interests.

Complications and Side Effects: Stenosis, regurgitation, endocarditis, hemolysis, thromboembolism, valve thrombosis, nonstructural dysfunction, structural valve deterioration, anemia, arrhythmia, hemorrhage, transient ischemic attack/stroke, congestive heart failure, myocardial infarction, angina, any of which could lead to reoperation, explantation, permanent disability, and death.

Warnings: Alternative therapies should be considered in the presence of conditions affecting calcium metabolism or when calcium containing chronic drug therapies are used, including children, adolescents, young adults, and patients on a high calcium diet or maintenance hemodialysis. Should be used with caution in the presence of severe systemic hypertension or when anticipated patient longevity is longer than the known longevity of the prosthesis.

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