Australian Government

Department of Health

MEDICAL SERVICES ADVISORY COMMITTEE

Application 1361

Transcatheter Aortic Valve Implantation

Decision Analytic Protocol

October 2014

Contents

List of Tables

List of Figures

Title of application

MSAC application 1361 – Transcatheter Aortic Valve Implantation

Purpose of application

Edwards LifeSciences (the applicant) are requesting Medicare Benefits Schedule (MBS) listing of transcatheter aortic valve implantation (TAVI) for use in patients who are symptomatic with severe aortic stenosis and who are determined to be at high risk for surgical aortic valve replacement or non-operable. The assessment of TAVI will be considered as a generic intervention i.e. clinical evidence and outcomes will be presented for all transcatheter valve types similar to the applicant's trademarked technology (Table 5).

Background

The proposed medical service is currently not funded under the MBS and has not been previously considered by the Medical Services Advisory Committee (MSAC). However, legal access to TAVI has been provided to patients under the following avenues:

- Special access scheme and authorised prescribers; and
- Participation in clinical trials and clinical registries.

Details of medical devices currently registered on the Australian Register of Therapeutic Goods (ARTG), which are associated with TAVI, are provided in the section "Regulatory information".

Medical condition and population eligible for the proposed intervention

Description of the medical condition

Aortic stenosis

Aortic stenosis is the progressive narrowing of the native aortic valve opening resulting in the obstruction of blood flow. A congenital malformation of the valve may also result in stenosis and is the more common cause in young adults (Bonow, Carabello et al. 2008). The pathophysiology of aortic stenosis includes an increase in afterload, progressive hypertrophy of the left ventricle, and a decrease in systemic and coronary blood flow as consequences of valve obstruction.

Aortic stenosis is the most common valvular heart disease in adults (Yan, Cao et al. 2010). Affected individuals are typically > 65 years of age. The Euro Heart Survey on Valvular Heart Disease was conducted in 2001 in 92 centres from 25 countries on 5,001 patients. The survey found among the single native left-sided valve disease, aortic stenosis was the most frequent (43.1% of patients) (Iung, Baron et al. 2003).

The natural history of aortic stenosis in the adult consists of a prolonged latent period during which morbidity and mortality are very low. After the latent period, symptoms of angina, syncope, or heart failure develop. Once the symptoms appear, average survival decreases rapidly with a high risk of sudden death (Varadarajan, Kappor et al. 2006; Bonow, Carabello et al. 2008).

Currently, the treatment options for patients with symptomatic aortic stenosis are standard (surgical) aortic valve replacement and medical management.

Standard aortic valve replacement involves cardiopulmonary bypass and median sternotomy incision (Vahanian, Alfieri et al. 2012) and is currently funded under the MBS. However, a significant proportion of patients over the age of 75 with severe aortic stenosis do not undergo standard aortic valve replacement due to risks arising from age and co-morbidities (Yan, Cao et al. 2010).

In patients managed conservatively (i.e. non-surgical management), the mortality rate is increased with age, heart failure, and renal insufficiency. Studies have found that severe aortic stenosis left untreated surgically results in a survival rate of 62% at year 1, 32% at year 5 and 18% at year 10 (Varadarajan, Kappor et al. 2006). There is a high risk of sudden death in patients with severe aortic stenosis if the diseased valve is not replaced.

Description of the proposed patient population

The proposed patient population are those who are symptomatic with severe aortic stenosis (aortic valve area < 1.0cm2) and who have been assessed by a specialist medical team to have high risk for operative mortality, or are 'non-operable', as determined by an objectively predicted operative mortality of at least 10% according to the Society of Thoracic Surgeons (STS) score or an equivalent validated scoring system. Patients with severe aortic stenosis may be determined to be at high-risk or contraindicated for surgical valve implantation due to factors such as advanced age or major left ventricular dysfunction, or the combination of comorbidities (Iung, Cachier et al. 2005).

Given the potential for considerable heterogeneity in defining both high risk and non-operable status across the population of patients who are symptomatic with severe aortic stenosis, objective risk scoring frameworks have been developed to determine the level of operative risk including the STS score and the European system for Cardiac Operative Risk Evaluation (EuroSCORE). Appendix 1 outlines the background of these scoring systems such as the cohort of patients and procedures that informed their formulation and the extent to which they accurately predict operative mortality in

individual patients being considered for TAVI. In general, studies have shown that the EuroSCORE overestimates the risk for operative mortality compared to the STS score (Parolari, Pesce et al. 2010; Basraon, Chandrashekhar et al. 2011) and as such should not be used to assess risk.

It is important to note that while the established risk scoring frameworks are important in the preoperative assessment of patients for aortic valve intervention, some patients may be considered too high risk / unsuitable for AVR but suitable for TAVI (Svensson, Adams et al. 2013). This would include patients with the following conditions:

- Advanced liver disease;
- Porcelain aorta;
- Complications with prior cardiac surgery (mediastinitis, prolonged intubation);
- Malignancy;
- Chest deformity (pectus excavatum, mastectomy, irradiation);
- Subdural hematoma;
- Blood dyscrasia;
- Refusal of blood products;
- Immobility;
- malnutrition.

The STS framework may not cover all conditions that a patient may have. Therefore, in addition to using a risk scoring framework as a guide to selecting patients, this application is also proposing that TAVI should only be undertaken with a multidisciplinary 'heart team'. This is expanded upon later in this document but the oversight from a multidisciplinary team is primarily designed to ensure consistency in patient selection and reduce variation across providers (as well as across institutions) in how patient's operative risk is determined and to ensure that the threshold for acceptable risk profile for TAVI remains aligned with its intended purpose. The applicant also notes that procedural guidelines have been recently developed and endorsed by the Cardiac Society (CSANZ) of Australia and New Zealand and the Australian New Zealand Society of Cardiac and Thoracic Surgeons (ANZSCTS).

Clinical evidence for the proposed population

This section presents a summary of clinical data relevant to a comparison of TAVI and standard aortic valve replacement and a comparison of TAVI and medical management in the proposed population with symptomatic aortic stenosis. The relevant trials are listed in Table 1 and the associated citations are listed in Appendix 2.

Table 1: List of relevant randomised control trials

Trials	Brief description
PARTNER trial: Placement of aortic transcatheter valve trial Edwards SAPIEN Transcatheter heart valve	**Description:** Ongoing interventional randomised study to determine the safety and effectiveness of the device and delivery systems (transfemoral and transapical) in high risk, symptomatic patients with severe aortic stenosis. Two patient populations were considered: Cohort A: Edwards Sapien valve (transfemoral or transapical) vs. other surgical valve. Cohort B: Edwards Sapien valve (transfemoral) vs. medical therapy. **Main citations:** Smith CR, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med. 2011; 364(23):2187-98. Leon MB, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med. 2010; 363(17): 1597-607.
Adams, 2014	**Description** Randomised control trial to determine the non-inferiority or superiority of transcatheter aortic-valve replacement using a self-expanding transcatheter aortic-valve bioprosthesis compared to surgical aortic-valve replacement in high risk symptomatic patients with severe aortic stenosis **Main citations** Adams DH, et al. Transcatheter Aortic-Valve Replacement with a Self-Expanding Prosthesis. N Engl J Med 2014, 370(19): 1790-1798

Estimated number of patients eligible for TAVI

The estimates regarding expected usage are derived from a number of sources, summarised in Table 2 below.

Table 2 Sources of data used to estimate the extent of TAVI use

Variables	Source
Australian population and population projections	Australian Bureau of Statistics (ABS)
Number of MBS claims for SAVR	MBS online (see Table 6)
Symptomatic severe AS not treated with SAVR	Osnabrugge et al (2013
Proportion of patients eligible for TAVI	Osnabrugge et al (2013)

AS = Aortic stenosis; SAVR = standard aortic valve replacement; pop. = population; TAVI = transcatheter aortic valve replacement.

Table 3 below presents the projections of the Australian population (≥65 years) between 2015 and 2019. The projections are based on the ABS population projections estimates (series B).

Table 3 Projections of Australian population (≥65 years) 2015 to 2019

	2015	**2016**	***2017***	***2018***	***2019***
Adult population (≥65 years)	3,567,519	3,686,083	3,804,770	3,929,281	4,053,834

Source: Australian Bureau of Statistics (2012) 31010.

Future SAVR procedures (in the absence of TAVI) was estimated based on the current proportion of SAVR procedures (MBS claim data for items 38488 and 38489) in the current population applied to

the predicted adult population. The proportion of these, which would be eligible (5.2%), is sourced from Osnabrugge et al (2013) as well as the proportion of those eligible who receive TAVI treatment (80%). The population of those with symptomatic severe AS not treated with SAVR is based on the relative proportions of those treated compared to those not treated provided in Osnabrugge et al (2013). Finally, the estimate of those treated with TAVI instead of not treated is estimated based on the proportion of those who would be eligible for TAVI (28.7%) and the total TAVI patients equal to the sum of those who receive TAVI instead of SAVR and those who receive TAVI instead of medical management. Table 4 below presents the estimates of patients eligible for TAVI treatment.

Table 4: Estimated patients considered eligible for TAVI treatment

	2015	2016	2017	2018	2019
Adult population (≥65 years)	3,087,911	3,221,312	3,360,476	3,505,652	3,657,100
SAVR procedures (MBS items 38488, 38489)	3,034	3,134	3,235	3,341	3,447
SAVR patients eligible for TAVI (5.2%)[a]	158	163	169	174	180
Eligible patients treated with TAVI instead of SAVR (80%)[a]	127	131	136	140	144
Symptomatic severe AS not treated with SAVR	2,066	2,134	2,202	2,275	2,347
Eligible patients treated with TAVI instead of MM (28.7%)[a]	593	613	632	653	674
Total TAVI patients	**720**	**744**	**768**	**793**	**818**

[a] *Osnabrugge et al 2013.*

Therefore, the number of patients eligible for TAVI is estimated at 720 in 2015 and rising to 818 in 2019.

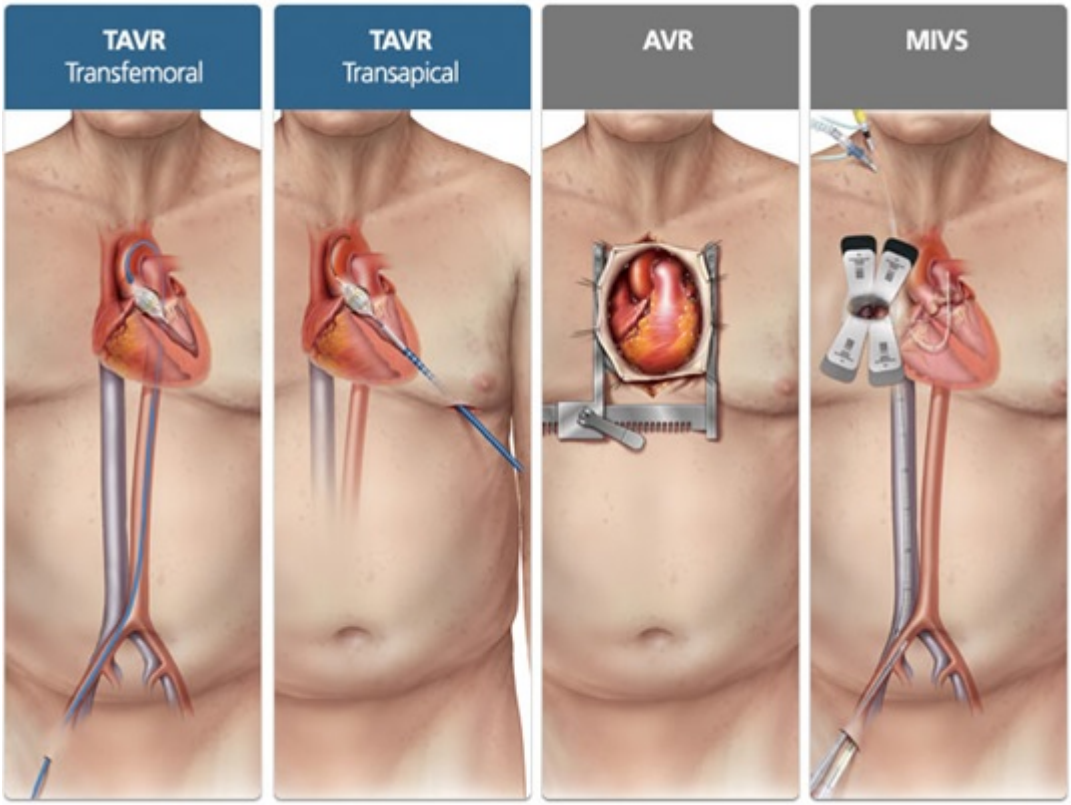
Whilst the estimated annual number of patients eligible for TAVI treatment is expected to rise over time (in line with an ageing population in Australia), the rate of symptomatic severe aortic stenosis within this patient population is not likely to increase. Moreover, because TAVI is a late stage intervention patients are generally not expected to undergo a second TAVI in their lifetime.

Intervention – proposed medical service

Description of the intervention

TAVI can be delivered via two different approaches: percutaneous peripheral access (i.e. transfemoral approach) or minimally invasive surgical approach (transapical, transaortic or sub-clavian). The various procedures are depicted in Figure 1.

Figure 1: Diagram of procedures



MIVS: Transaortic via subclavian or ministernotomy

TAVI is usually performed under general anaesthesia; however, sedation and analgesia may suffice for the transfemoral approach (Vahanian, Alfieri et al. 2008).

Percutaneous peripheral access available

The transfemoral procedure is performed by the retrograde femoral approach with fluoroscopic and transoesophageal echocardiographic guidance and without cardiopulmonary bypass. A percutaneous sheath is carefully inserted into the femoral artery. After retrograde crossing of the aortic valve and pre-dilation of the native valve with conventional balloon aortic valvuloplasty (performed under rapid pacing), the balloon-mounted bioprosthesis is advanced through the aorta and positioned within the native aortic annulus using a specialised delivery system. The valve is subsequently expanded under rapid pacing to minimise transvalvular flow, cardiac motion, and the risk for valve embolisation.

Peripheral access not available (surgical approach)

The transfemoral approach can be either prepared surgically or approached percutaneously. In a majority of cases these procedures are performed percutaneously as described above.

The transapical procedure should be performed in an operating theatre or hybrid operating theatre that includes optimal imaging with a high-quality fluoroscopic system equivalent to that of a cardiac catheterisation laboratory with a large image intensifier and immediate replay capability. Access to the aortic valve is achieved surgically via an anterolateral mini-thoracotomy placed in the fifth or possibly sixth intercostal space, followed by apical puncture of the left ventricle. An epicardial pacing wire is placed and tested for pacemaker capture. Two large purse string sutures with pledgets are placed at the left ventricular apex. After puncturing the apex followed by subsequent pre-dilation of the native valve with conventional BAV, the aortic bioprosthesis crimped on a specialised delivery system and is advanced and positioned using fluoroscopic, aortographic and echocardiographic guidance. The valve is then expanded and deployed under rapid pacing to minimise transvalvular flow, cardiac

motion, and the risk for valve embolisation. The ventricular sheath is removed and haemostasis secured with the previously placed pledgeted sutures.

Patients who are deemed non-operable for open surgery are deemed still operable for the transapical approach. Unlike open surgery, minimally invasive procedures do not require bypass. Transfemoral is the preferred approach unless contraindicated by other factors. Following the clinical algorithm, transfemoral is considered first, and if femoral access is not viable then minimally invasive surgical approaches are considered.

The transaortic and sub-clavian procedures are alternative surgical approaches if the patient's anatomy prevents a transfemoral approach. These procedures should be performed in a cardiac catheterisation laboratory or a hybrid laboratory.

Given the potential differences in resource utilisation between transfemoral and minimally invasive surgical procedures, separate economic analyses will be conducted for each approach. Evidence will be provided with respect to the proportion of TAVI procedures expected to be transfemoral compared to minimally invasive surgical procedures.

Imaging services

During these procedures, peri-procedural transoesophageal echocardiography monitoring can be used to assist in the positioning of the prosthetic valve as well as to detect complications. The following imaging methods can also be used to position the prosthesis at the aortic valve (Vahanian, Alfieri et al. 2008):

- Fluoroscopy to assess the level of valve calcification;
- Aortography performed at the beginning of the procedure and eventually repeated with the undeployed prosthesis to determine the position of the valve and the plane of alignment of the aortic cusps;
- Echocardiography.

When the positioning is considered correct, the prosthesis is released. Immediately after the procedure, aortography and echocardiography are performed to assess the location and degree of aortic regurgitation and the patency of the coronary arteries. After the procedure, the patients can either be transferred to a coronary care unit, high dependency or intensive care where they are monitored for haemodynamics, vascular access, rhythm disturbances and renal function.

Clinical place for proposed intervention

TAVI should be established in high volume cardiac surgical centres where on site valve surgery is performed. The following institutional requirements are suggested for undertaking TAVI programs:

- Institutional interventional program: 1000 catheter studies/400 PCI per year;
- Institutional surgical program:
  - 50 total aortic valve replacement per year of which at least 10 aortic valve replacements should be high risk (STS≥6);
  - Minimum of two institutionally-based cardiac surgeons in program

Comparison of trademarked health technology

The proposed medical service includes a specific trademarked health technology: the Edwards SAPIEN valve. Similar health technologies include the CoreValve ReValving system and the Boston's SADRA valve. Table 5 below outlines the technical specifications of each trademarked technology, and Appendix 3 describes the various platforms used for TAVI in Australia and New Zealand.

Table 5 Technical specifications of the Edwards SAPIEN valve, the CoreValve system, and the Boston's SADRA valve

	Edwards SAPIEN	Medtronic CoreValve	Boston's SADRA valve
Valve specifications	Balloon-expandable, tubular, slotted, stainless steel stent with an attached bovine pericardial trileaflet valve and fabric sealing cuff	Self-expanding 50mm nitinol frame sewn to three porcine pericardial leaflets; prosthesis has three separate structural elements (inlet, middle and outlet)	Braided Nitinol Stent with radial expansion as frame shortens.
Delivery method	Valve is mechanically crimped onto a balloon catheter immediately prior implantation	Valves are manually crimped onto the delivery system and then covered by outer sheath	Valves are loaded onto the delivery system and then covered by outer sheath
Rapid ventricular pacing requirement	To stabilise the prosthesis during balloon expansion, rapid pacing needed (160 - 220 beats/min)	Used to stabilise the prosthesis during deployment (rapid pacing 160-220 beats/min)	Used To stabilise the prosthesis during deployment (rapid pacing 160-220 beats/min).
Delivery sheath size	22F (7.3mm) and 24F (8mm); 18F (6mm)	18F (6mm)	18F (6mm)
Methods of deployment	Antegrade (Transapical) &, Retrograde (Transfemoral)	Retrograde (transfemoral and subclavian)	Retrograde (Transfemoral)
Potential advantages	Discrete height does not impinge on conductive system. Design modelled on traditional heart valve manufacturing materials and techniques Prosthesis can be re-expanded if under-deployed initially	Self-expanding deployment	Enables device repositioning or retrieval prior to complete deployment of the valve. Adaptive seal.

Source: Table 2, p521 (Layland, Bell et al. 2010)

Rural access

Considering the institutional requirements to perform TAVI, patients from rural and remote areas will have to travel to sites where TAVI can be performed.

Frequency of use

The patient is not expected to undergo another TAVI during their lifetime.

Delivery of the proposed intervention

TAVI should only be undertaken with a multidisciplinary 'heart team'. The multidisciplinary team would include the following core members in line with the recent position statement from The Cardiac Society of Australia and New Zealand and the Australian and New Zealand Society of Cardiac & Thoracic Surgeons:

- Interventional cardiologist;
- Cardiothoracic surgeon;
- TAVI nurse case manager/co-ordinator.

The multidisciplinary team may also include: imaging cardiologist or radiologist, general cardiologist, cardiac anaesthetist, intensive care physician, geriatrician or general physician, or vascular surgeon.

The final construction of the heart team should include a broad range of health professionals providing all the necessary skills and expertise to fully assess patients who are potential TAVI candidates, provide balanced judgment about the most appropriate procedure in patients deemed appropriate for an aortic valve intervention, guide and perform a TAVI if indicated and support the patient peri-procedurally (CSANZ & ANZCTS, 2014)

Requirements for the interventional cardiologist

The interventional cardiologist should be trained in accordance with the Cardiac Society of Australia and New Zealand (CSANZ) guidelines. The current generation of devices requires two operators (primary and secondary) and the recommendations should apply to both. A background in structural intervention is considered an important pre-requisite for the competency in TAVI. The clinical experience of the interventional cardiologist should include but is not limited to:

- Coronary diagnostic procedures,
- Coronary interventions,
- Peripheral vascular diagnostic procedures,
- Peripheral vascular interventions,
- Balloon aortic, mitral, and pulmonic valve dilatation,
- Stent implantation in right ventricle outflow tract and pulmonary arteries,
- Intra-aortic balloon pump, other cardiac support,
- Device placement, including initiation of percutaneous cardiopulmonary;
- Percutaneous ventricular assist device placement;
- Endovascular aneurysm repair or thoracic endovascular aortic repair;
- Transeptal techniques,
- Coronary sinus access,
- Large vessel access and closure,

For an interventional cardiologist who has never performed TAVI, the following pre-requisites are suggested:

- 100 structural procedures lifetime, OR
- 20 left sided structural procedures per year of which at least 10 should be balloon aortic valvuloplasty procedures.

Left sided procedures include endovascular aneurysm repair, thoracic endovascular aortic repair, balloon aortic valve, aortic valve and mitral valve prosthetic leak closures and ventricular septal defect closures. Left sided procedures do not include atrial septal defect/patent foramen oval closure.

Further, the interventional cardiologist should have been trained and proctored on the devices being used. For an operator who has never implanted a transcatheter valve, a minimum of ten proctored cases in which the primary and secondary operators are working as a team, is recommended.

Requirements for the cardiac surgeon

The TAVI surgeon should be experienced in surgical aortic valve replacement (AVR) with experience in operating on high-risk surgical AVR patients. The surgeon should have experience in obtaining access via transapical and less invasive routes such as hemi-sternotomy. Experience with open exposure and access to the iliac arteries is desirable.

The following experience and training is recommended:

- 100 AVR career, at least 10 of which are 'high-risk', OR
- 25 AVR per year, OR
- 50 AVR in two years, AND
- At least 20 AVR in last year prior to TAVI initiation,
- Experience with, and management of, peripherally inserted cardiopulmonary bypass,
- Experience with open retroperitoneal exposure of, and surgical intervention on, the iliac arteries,

The surgeon should also have been trained and proctored on the devices being used. For a surgeon who has never implanted a transcatheter valve, a minimum of ten proctored cases in which the primary and secondary operators are working as a team, is recommended.

Required training

A successful pre-training plan includes:

- Building a collaborative team.
- Defining the procedure location with the required room ventilation and imaging
- equipment, such as modified catheterisation laboratory or hybrid operating room.
- Identifying and evaluating which patients qualify for this innovative procedure to ensure a minimum caseload to maintain skills.

The applicant advises that it provides a comprehensive and hands-on training program. The whole team including cardiac surgeons, interventional cardiologists, echocardiographers, anaesthetists, nurses and technicians are trained together. The program consists of the following mandatory modules:

1. An electronic training package that contains educational material, case studies screening advice and tools, and device handling instructions.
2. Didactic sessions and curriculum: as TAVI is an emerging field with new sets of challenges, didactic sessions are to be conducted by experts in TAVI procedures and are to focus on

patient selection, procedural steps, best practices, complications, troubleshooting and careful review of TAVI case studies.

3. TAVI procedure observation requirement: prior to procedural training (proctoring), each interventional cardiologist and heart surgeon is required to observe at least one TAVI procedure. Specifically, trainees must watch one transfemoral TAVI procedure to train on the retrograde approach and one transapical TAVI procedure to train on the transapical approach.
4. Simulator training: prior studies have demonstrated using metric-based simulation training for surgical procedures has been beneficial. Metric-based simulations on transfemoral and transapical procedures are utilised to acquire technical skills related to TAVI in real-world situational experiences but without the risk to patients. Patient cases vary with differing levels of difficulty and offer both diagnostic and procedural challenges through real patient fluoroscopic imaging and responsive haemodynamic feedback.
5. THV equipment in service: the Sponsor THV Clinical specialists will conduct hands-on in-services of all TAVI equipment. In-service training includes a detailed review of procedural steps to correctly mount, crimp and orient a bioprosthesis onto a balloon cathether.
6. Device preparation: nurses or technicians will be certified for transapical and transfemoral delivery systems and valve preparation.
7. Patient review; 6 cases or patient files are brought and reviewed during training to validate indications and define the most appropriate approach for patient treatment.
8. Procedure proctoring: based on a successful completion of requirements and criteria documented in modules 1 to 4 above, physicians may progress to final phase of training (proctoring). A minimum of two successful proctored cases per TA and per TF are required to become independent operators in performing TAVI procedures, and eight independent procedures to become a proctor. Following proctoring, clinical support will be provided for an additional 10 to 15 cases. The sponsor of the trademarked technology will continue to provide clinical specialist support for all ongoing consultations with the heart team.
9. Dry runs are conducted in the procedural area prior to the institutions first case being conducted. All personnel and equipment involved in the procedure are placed in the lab/OT to ensure smooth procedural flow and the location of any emergency devices or equipment.

Upon completion of this educational program, each participant is certified to perform TAVI (transfemoral and transapical) procedures successfully.

Regulatory information

Details of medical devices currently registered on the ARTG, which are associated with TAVI, are as follows:

215465: Edwards Lifesciences Pty Ltd – Edwards SAPIEN Transcatheter Heart Valve (THV) Model 9000TFX with Ascendra Delivery System – Cardiac valve graft, animal-derived.
Intended for use in patients with symptomatic aortic stenosis (aortic valve area<0.8cm2) requiring aortic valve replacement who have high risk for operative mortality, or are 'non-operable', as determined by an objectively predicted operative mortality of at least 10% according to STS or an equivalent validated scoring system. Decision for use should be reviewed by three independent medical specialists, including one cardiologist and one cardiothoracic surgeon.

215298: Edwards Lifesciences Pty Ltd – Edwards SAPIEN Transcatheter Heart Valve (THV) Model 9000TFX with RetroFlex 3 Delivery System – Cardiac valve graft, animal derived.
Indicated for use in patients with symptomatic aortic stenosis (aortic valve area<0.8cm2) requiring aortic valve replacement who have high risk for operative mortality, or are 'non-operable', as determined by an objectively predicted operative mortality of at least 10% according to STS or an equivalent validated scoring system. Decision for use should be reviewed by three independent medical specialists, including one cardiologist and one cardiothoracic surgeon.

Comparator

The Protocol nominates two appropriate comparators (as discussed below):

- Standard (surgical) aortic valve replacement; and
- Medical management (± balloon valvuloplasty).

Standard aortic valve replacement (SAVR)
The proposed intervention is likely to substitute standard aortic valve replacement in patients not contraindicated for SAVR but at high risk for SAVR. These patients can undergo SAVR or TAVI based on the assessment by the multidisciplinary team. Therefore for this patient group, standard aortic valve replacement is the nominated comparator.

Standard aortic valve replacement is already publicly funded under the MBS items 38488 and 38489.

Table 6 MBS item for standard aortic valve replacement

MBS item	Description	Schedule Fee	Number of claims		
			2011	2012	2013
38488	Valve replacement with bioprosthesis or mechanical prosthesis	$1,909.60	2,579	2,676	2,795
38489	Valve replacement with allograft (subcoronary or cylindrical implant) or unstented xenograft	$2,271.05	47	60	45

Source: MBS online. Schedule fee as at 26 February 2014

Medical management (± balloon valvuloplasty)
The proposed intervention is also expected to be used in patients who are treated medically. This would be for patients contraindicated for SAVR. Patients contraindicated for SAVR would usually have medical treatment. Therefore, the nominated comparator for this patient population is medical treatment. Some patients receiving medical management may undergo balloon valvuloplasty.

Expected health outcomes relating to the medical service

Health outcomes will be measured in order to assess the safety and effectiveness of the proposed intervention and appropriate comparators.

Primary effectiveness outcomes for the proposed intervention and comparators include improvement in patients' quality of life and life expectancy.

Second effectiveness outcomes for the proposed intervention and comparators include:

- Improved renal function,
- Length of hospital stay,
- New York Heart Association (NYHA) Functional status,
- Health care resource utilisation post-procedure,
- Improved haemodynamic results
- Performance/placement of TAVI (e.g. paravalvular leak, subsequent pacemaker).

Safety outcomes include any adverse events related to the proposed intervention and the comparators. The assessment of safety for TAVI, standard aortic valve replacement and medical management could include:

- Stroke,
- Vascular complications
- Major bleeding
- Acute kidney injury.

Type of economic evaluation

It is proposed that there will be a total of four economic evaluations: one for each indication and comparator for both transfemoral and minimally invasive surgical procedures:

- Transfemoral procedure (i.e. when percutaneous peripheral access is available)
  - Cost-effectiveness analysis of TAVI versus standard aortic valve replacement in patients with high-risk for operative mortality;
  - Cost-effectiveness analysis of TAVI versus medical management in patients who are otherwise non-operable.
- Minimally invasive surgical procedure (i.e. when percutaneous peripheral access is NOT available)
  - Cost-effectiveness analysis of TAVI versus standard aortic valve replacement in patients with high-risk for operative mortality;
  - Cost-effectiveness analysis of TAVI versus medical management +/- balloon valvuloplasty in patients who are otherwise non-operable.

The approach for each economic evaluation described below is preliminary and will likely be modified according to data availability.

Cost-effectiveness of TAVI (transfemoral or minimally invasive surgery) versus standard aortic valve replacement in patients with high-risk for operative mortality

A cost-effectiveness evaluation is performed comparing TAVI versus standard aortic valve replacement. The health benefits associated with TAVI over standard aortic valve replacement reflect improved quality of life as well as improved life expectancy.

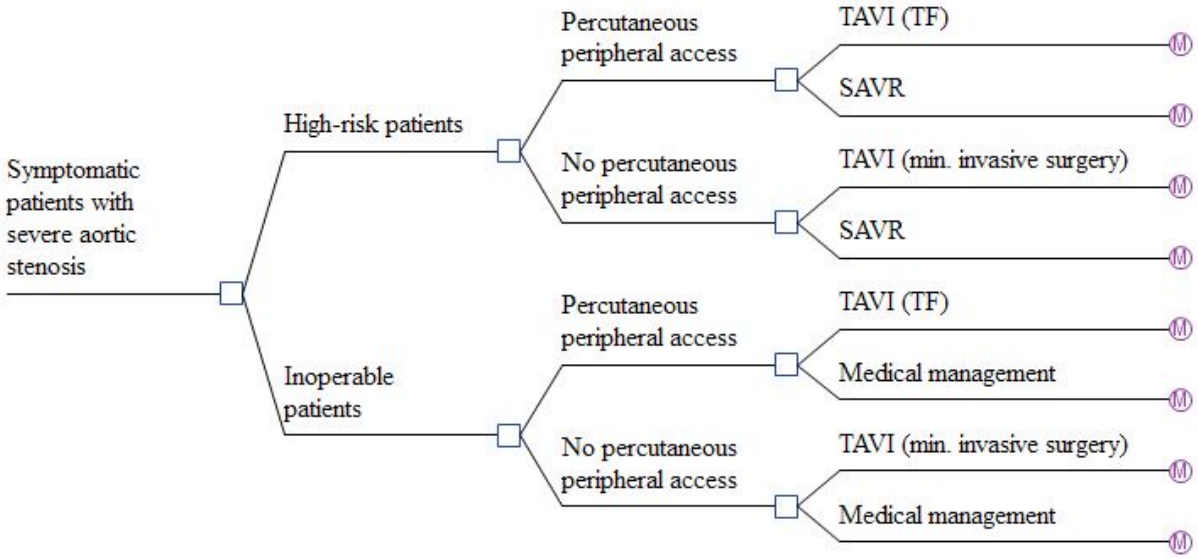
Cost-effectiveness of TAVI (transfemoral or minimally invasive surgery) versus medical management +/- balloon valvuloplasty **in patients who are non-operable**

A cost-effectiveness evaluation is performed comparing TAVI versus medical management. The economic evaluation should model the medical management treatment arm with and without balloon valvuloplasty, as these will have different weights and costs.

The health benefits associated with TAVI over medical management +/- balloon valvuloplasty are likely to be improved quality of life and improved life expectancy.

The decision analytic model will be structured as follows:

Figure 2: Decision analytical model



TAVI: transcatheter aortic valve implantation; SAVR: standard aortic valve replacement; TF: transfemoral;

Proposed MBS item and fee

The proposed medical service is likely to substitute standard aortic valve replacement in patients considered eligible by the heart team. Standard aortic valve replacement is already publicly funded under the following MBS items: 38488 and 38489.

The proposed fee for the intervention is based on item 38488 ‘valve replacement with bioprosthesis or mechanical prosthesis’ with a fee of $1,909.60 (as of 20 February 2014).

The proposed item and fee are described below.

Table 7 Applicant's proposed MBS item descriptor for TAVI

Category 3 – Therapeutic Procedures
MBS XXXXX Transcatheter aortic valve replacement for the treatment of symptomatic severe aortic stenosis in a suitable patient formally assessed by a heart MDT to have an unacceptably high risk for surgical aortic valve replacement. (Anaes.) (Assist.) (i) Percutaneous approach Explanatory notes A 'heart team' team is required to formally document approval regarding the patient's suitability for treatment. The core personnel of the heart team should include an interventional cardiologist, 2 cardiothoracic surgeons, a transoesophageal echocardiologist, an anaesthetist, a geriatrician and a TAVI nurse / case manager. The multi-disciplinary extended team should additionally include: a general cardiologist, an intensive care physician and a radiologist.
Category 3 – Therapeutic Procedures
MBS XXXXX Transcatheter aortic valve replacement for the treatment of symptomatic severe aortic stenosis in a suitable patient formally assessed by a heart MDT to have an unacceptably high risk for surgical aortic valve replacement. (Anaes.) (Assist.) (ii) Minimally invasive surgical approach Explanatory notes A 'heart team' team is required to formally document approval regarding the patient's suitability for treatment. The core personnel of the heart team should include an interventional cardiologist, 2 cardiothoracic surgeons, a transoesophageal echocardiologist, an anaesthetist, a geriatrician and a TAVI nurse / case manager. The multi-disciplinary extended team should additionally include: a general cardiologist, an intensive care physician, and a radiologist.

Health care resources

Consumable component

The consumables used for the proposed service are listed in Table 7 below. The use and quantity are likely to differ by procedure (transfemoral and minimally invasive surgery). The costs were not available for all items. Where applicable, the unit cost is provided in the last column.

Table 8 List of consumables for a transcatheter aortic valve implantation

Item	Quantity	Price per pack	Quantity per pack	Unit cost
Standard angiogram pack	1	$392	4	$98
7 French sheaths	3	$120	10	$1.20
E.P add on kit	1	$299	5	$59.80
Hi pressure line for injector	1	$134.40	20	$6.72
Hi pressure 3-way taps	2	NA		NA
6 French FR4 diagnostic catheter	1			
6 French PIG catheter	1	$51	5	$10.20
6 French JL4	1 (on-hand)	$51	5	$10.20
AL1 diagnostic catheter	1 (on-hand)	$51	5	$10.20
6 French proglides	2	$3200	10	$320
0.35 J Wire	1			$16
0.35 straight wire 145cm length	1			$20
Amplatz extra stiff exchange J wire	1			$90
Winged Cook needle 7 cm	1			$10
Temporary pacing electrode catheter and bridging cable	1	$900	5	$180
Sterile huck towels	7	NA		
2.0 silk suture	1	NA		
Disposable suture sets	2	$104.81	25	$4.20
50ml Luer lock syringe	1	NA		
30ml Luer lock syringe	4	NA		
150ml Gallipot	3	$14.88	25	$0.60
>500ml sterile bowls	4	$34.50	12	$2.88
Sterile gauze	2	$37.56	50	$0.75
Moquito clips	4	$124.88	100	$1.25
Towel clips	4	NA		
Adhesive table cover (160x240) from theatre	1	NA		
Adhesive drape sheet (from theatre)	1	NA		
Lead screen covers	2	$210	50	$4.20
II covers	2	$87.80	40	$2.20
Big lead screen cover	1	$135	50	$2.70
1000ml normal saline solution	2	NA		
1000ml normal saline solution with 20000 units heparin	1	NA		
Pressure bags (one with 200ml contrast and one with 100ml contrast injector 100mls)	2	NA		

Equipment component

The facilities should include but are not limited to the following:

1. Cardiac catheterisation laboratory or hybrid operating room. The catheterisation laboratory should be equipped with a fixed radiographic imaging system with high resolution fluoroscopy;
2. Non-invasive imaging:
    - Echocardiographic laboratory with transthoracic and transoesophageal echocardiographic capabilities and with sonographers and echocardiographers experienced in valvular heart disease;
    - Access to a vascular laboratory (non-invasive) with vascular specialists capable of performing and interpreting vascular studies;
    - Access to a CT laboratory with CT technologists and specialists who can acquire and interpret cardiac CT studies.
3. A sterile environment that meets standards of an operating room or for pacemaker/ICD implantation:
    - sufficient space to accommodate the necessary equipment for uncomplicated implantations;
    - space for anaesthesiology, echocardiography, and cardiopulmonary and bypass equipment and personnel;
    - circulating heating, ventilation, and air conditioning laminar flow diffusers (this is desirable but will not be available in most current interventional cardiology suites); and
    - asymmetrical/symmetrical six-lamp 2 - 4 troffers (the inverted, usually metal trough suspended from the ceiling as a fixture for fluorescent lighting) to provide adequate high-output lighting for surgical intervention. (This is desirable but will not be available in most current interventional cardiology suites).
4. Capability of running cardiopulmonary bypass.
5. Operation of an anaesthesia machine.
6. Adequate room size to accommodate the standard equipment required in a cardiac catheterisation laboratory
7. Interventional Equipment: appropriate equipment for the procedure and for dealing with possible complications should be stocked.
8. A post procedure intensive care facility, high dependency unit (HDU) or coronary care unit (CCU) experienced in managing complex cardiac patients, including patients following conventional cardiac surgery.

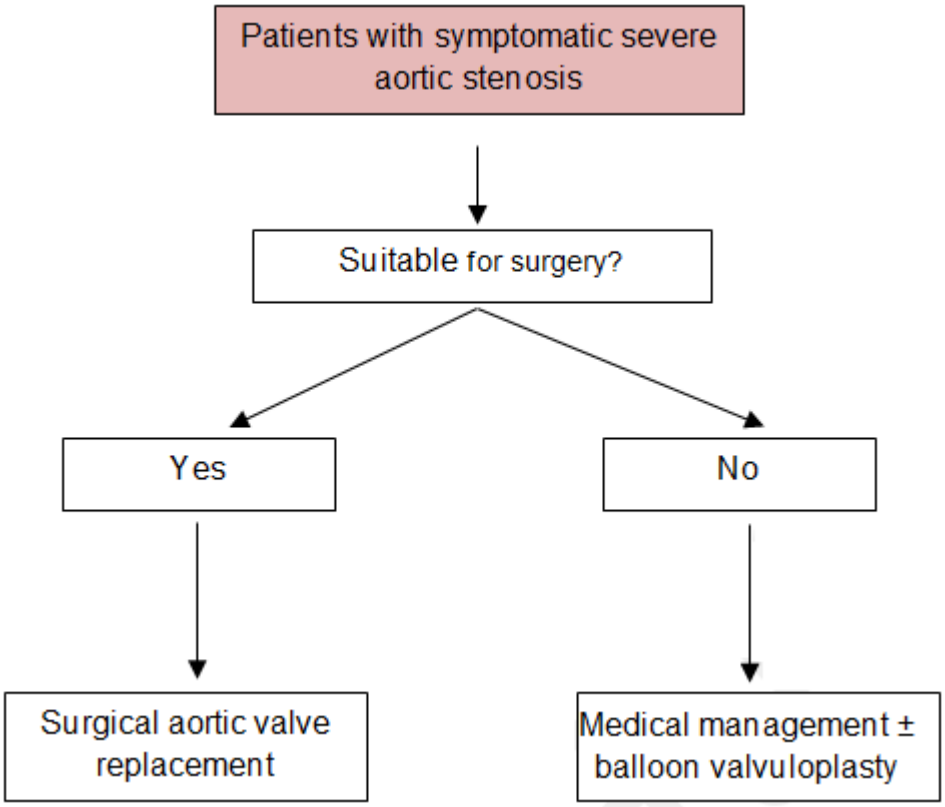
As the proposed service should only be established in high volume cardiac surgical centres where on site valve surgery is performed, the direct costs of equipment is not expected to be different from facilities that perform valve surgery.

A summary of the resources to be considered in the economic analysis is presented in Table 10.

Clinical Management Algorithms

The current clinical management algorithm for the defined patient population is presented in Figure 3. The current clinical management algorithm is based on the ECS/EACTS guidelines for the management of severe aortic stenosis (Vahanian, Alfieri et al. 2012).

Figure 3 Current clinical management algorithm



The proposed clinical management algorithm for the defined patient population is presented in Figure 4. The proposed clinical management algorithm follows the ECS/EACTS 2012 guidelines for the management of severe aortic stenosis (Vahanian, Alfieri et al. 2012).

Figure 4 Proposed clinical management algorithm

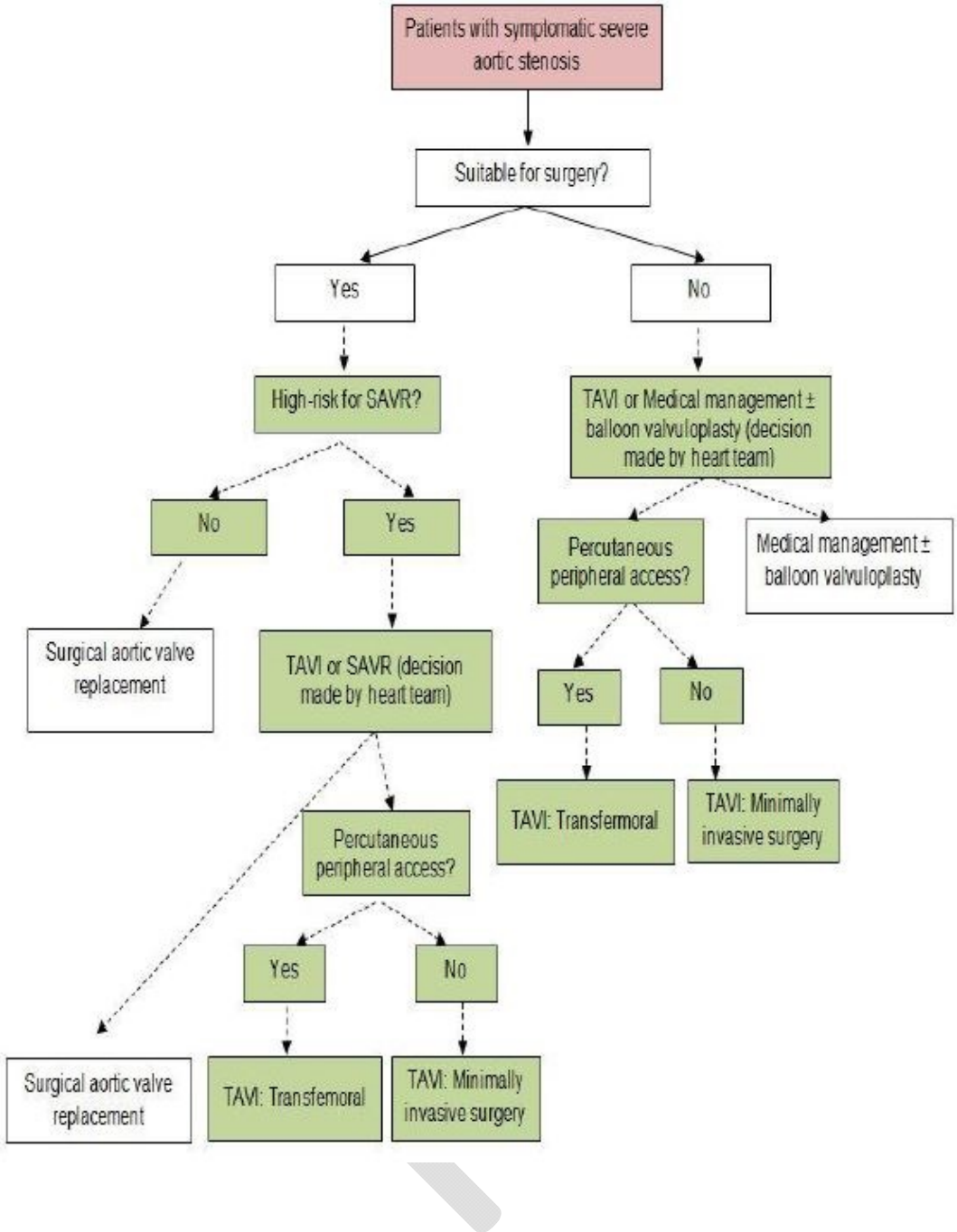


Table 9 Summary of PICO to define research question

Population	Intervention	Comparator	Outcomes to be assessed	Health care resources to be considered
Patients at high risk for operative mortality & percutaneous peripheral access is available	TAVI – transfemoral	Standard AVR	Improvement in overall survival. Impact on quality of life	Cost of intervention and comparator. Cost of management of adverse events. Cost of follow-up management.
Patients who are non-operable but do not have a short life expectancy & percutaneous peripheral access is available	TAVI – transaortic / transapical / sub-clavian	Medical management ± balloon valvuloplasty	Improvement in overall survival. Impact on quality of life	Cost of intervention and comparator. Cost of management of adverse events. Cost of follow-up management.
Patients at high risk for operative mortality & percutaneous peripheral access is NOT available	TAVI - transfemoral	Standard AVR	Improvement in overall survival. Impact on quality of life	Cost of intervention and comparator. Cost of management of adverse events. Cost of follow-up management.
Patients who are non-operable but do not have a short life expectancy & percutaneous peripheral access is NOT available	TAVI - transaortic / transapical / sub-clavian	Medical management ± balloon valvuloplasty	Improvement in overall survival. Impact on quality of life	Cost of intervention and comparator. Cost of management of adverse events. Cost of follow-up management.

Table 10 List of resources to be considered in the economic analysis

	Provider of resource	Setting in which resource is provided	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
				MBS [a] (*item number in brackets)*	Safety nets*	Other government budget	Private health insurer	Patient	Total cost [b]
Resources provided to identify eligible population									
Electrocardiography	Echocardiographer	Outpatient		$26.60 (11700)		$0.00	$0.00	$4.65	$31.25
Chest x-ray	Radiologist	Outpatient		$40.10 (58503)		$0.00	$0.00	$7.15	$47.15
Transthoracic echo	Radiologist	Outpatient		$196.10 (55113, 55114, 55115)		$0.00	$0.00	$34.55	$230.65
Resources provided to deliver TAVI (transfemoral or minimally invasive surgery)									
CT Scan	Radiologist	Outpatient		$399.50 (57341, 57345)				$70.50	$470.00
Prosthesis (device and delivery system)	Interventional cardiologist	Delivery							
TAVI procedure	Interventional cardiologist	Delivery							
Surgical assistant (MBS 51303)	Interventional cardiologist	Delivery							
Transeosophageal electrocardiography	Echocardiographer	Delivery		$144.50 (55130)		$0.00	$0.00	$25.50	$170.00
Catheterisation / hybrid lab	Hospital	Delivery							

	Provider of resource	Setting in which resource is provided	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
				MBS [a] (*item number in brackets)*	Safety nets*	Other government budget	Private health insurer	Patient	Total cost [b]
Fluoroscopy	Technician	Delivery		$220.10 (61109, 61110)		$0.00	$0.00	$38.80	$258.90
Resources provided in association with TAVI (transfemoral or minimally invasive surgery)									
Intensive care unit management	Hospital	Pre-discharge		$271.60 [c] (13870)		$0.00	$0.00	$90.50	$362.10
Coronary care unit	Hospital	Pre-discharge							
General care	Hospital	Pre-discharge							
Ward nursing	Hospital	Pre-discharge							
Pharmacy	Hospital	Pre-discharge							
Transthoracic echocardiography	Cardiologist	Pre-discharge		$196.10 (55113, 55114, 55115)		$0.00	$0.00	$34.55	$230.65
Resources provided to deliver SAVR (surgical aortic valve replacement)									
Prosthesis (device and delivery system)	Surgeon/ cardiologist	Delivery							
Surgical procedure	Surgeon / cardiologist	Delivery							
Anaesthesiology	Anaesthesiologist	Delivery							
Perfusion	Perfusionist	Delivery							

	Provider of resource	Setting in which resource is provided	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
				MBS [a] (*item number in brackets)*	Safety nets*	Other government budget	Private health insurer	Patient	Total cost [b]
Transeosophageal electrocardiography	Echocardiographer	Delivery		$144.50 (55130)		$0.00	$0.00	$25.50	$170.00
Operating theatre	Hospital	Delivery							
Resources provided in association with SAVR (surgical aortic valve replacement)									
Intensive care unit management	Hospital	Pre-discharge		$271.60 [c] (13870)		$0.00	$0.00	$90.50	$362.10
ICU subsequent management	Hospital	Pre-discharge		$201.45 [c] (13873)		$0.00	$0.00	$67.15	$268.60
Coronary care unit	Hospital	Pre-discharge							
General care	Hospital	Pre-discharge							
Ward nursing	Hospital	Pre-discharge							
Pharmacy	Hospital	Pre-discharge							
Transthoracic echocardiography	Cardiologist	Pre-discharge		$196.10 (55113, 55114, 55115)		$0.00	$0.00	$34.55	$230.65
Resources provided to deliver medical management									
Balloon valvuloplasty	Surgeon/ cardiologist	Delivery		$836.10 (38270)		$0.00	$0.00	$76.20	$912.30

	Provider of resource	Setting in which resource is provided	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
				MBS [a] (*item number in brackets)*	Safety nets*	Other government budget	Private health insurer	Patient	Total cost [b]
Anaesthesiology	Anaesthesiologist	Delivery							
Operating theatre	Hospital	Delivery							
Resources used to manage patients successfully treated with TAVI (transfemoral or minimally invasive surgery)									
Pharmacy	Hospital	Post-discharge							
Specialist visit	Cardiologist	Post-discharge							
Echocardiography	Echocardiographer	Post-discharge	1 x 30-day follow-up; 1 x 6-month follow-up; 1 x 12-month follow-up; 1 x yearly follow-up	$26.60 (11700)		$0.00	$0.00	$4.65	$31.25
Resources used to manage patients who are unsuccessfully treated with TAVI (transfemoral or minimally invasive surgery)									
Pharmacy	Hospital	Post-discharge							
Specialist visit	Cardiologist	Post-discharge							
Transthoracic echocardiography	Cardiologist	Post-discharge	1 x 30-day follow-up; 1 x 6-month follow-up; 1 x 12-month follow-up; 1 x yearly follow-up	$196.10 (55113, 55114, 55115)		$0.00	$0.00	$34.55	$230.65
Echocardiography	Echocardiographer	Post-discharge	1 x 30-day follow-up; 1 x 6-month follow-up; 1 x 12-month follow-up; 1 x yearly follow-up	$26.60 (11700)		$0.00	$0.00	$4.65	$31.25

	Provider of resource	Setting in which resource is provided	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
				MBS [a] (*item number in brackets)*	Safety nets*	Other government budget	Private health insurer	Patient	Total cost [b]
Resources used to manage patients successfully treated with SAVR (surgical aortic valve replacement)									
Pharmacy	Hospital	Post-discharge							
Specialist visit	Cardiologist	Post-discharge							
Echocardiography	Echocardiographer	Post-discharge	1 x 30-day follow-up; 1 x 6-month follow-up; 1 x 12-month follow-up; 1 x yearly follow-up	$26.60 (11700)		$0.00	$0.00	$4.65	$31.25
Resources used to manage patients who are unsuccessfully treated with SAVR (surgical aortic valve replacement)									
Pharmacy	Hospital	Post-discharge							
Specialist visit	Cardiologist	Post-discharge							
Transthoracic echocardiography	Cardiologist	Post-discharge	1 x 30-day follow-up; 1 x 6-month follow-up; 1 x 12-month follow-up; 1 x yearly follow-up	$196.10 (55113, 55114, 55115)		$0.00	$0.00	$34.55	$230.65
Echocardiography	Echocardiographer	Post-discharge	1 x 30-day follow-up; 1 x 6-month follow-up; 1 x 12-month follow-up; 1 x yearly follow-up	$26.60 (11700)		$0.00	$0.00	$4.65	$31.25

* Include costs relating to both the standard and extended safety net.
[a] applying a 85% benefit to the relevant MBS item fee.
[b] Actual MBS item fee as of 25th February 2014.
[c] applying a 75% benefit to the relevant MBS item fee.

Appendix 1

The Society of Thoracic Surgeons' (STS) risk models predicts the risk of operative mortality and morbidity after adult cardiac surgery based on the patient demographic and clinical variables. For the surgical procedures, the STS currently has the valve model, the coronary artery bypass surgery (CABG) model and the valve+CABG model. For the valve model, there is a model for isolated aortic valve replacement (The Society of Thoracic Surgeons 2014). This specific model requires the following information:

1. Demographics: age and gender;
2. Risk factors: weight, height, diabetes, last creatine level preop, dialysis, hypertension, infectious endocarditis, chronic lung disease, immunosuppressive therapy, peripheral vascular disease, cerebrovascular disease;
3. Previous interventions: previous coronary artery bypass, previous valve, previous other cardiac interventions;
4. Preoperative cardiac status: myocardial infarction, cardiac presentation on admission, congestive heart failure, cardiogenic shock, resuscitation, arrhythmia;
5. Preoperative medications: inotropes;
6. Hemodynamics and cath: number of disease coronary vessels, left main disease ≥ 50%, ejection fraction, aortic stenosis, mitral stenosis, aortic insufficiency, mitral insufficiency, tricuspid inefficiency;
7. Operative: incidence and status; and
8. Mechanical cardiac assistance device.

With this information, the STS Risk Calculator (The Society of Thoracic Surgeons 2014) allows a user to calculate a patient's risk of mortality and other morbidities (e.g. length of stay, renal failure).

The European System for Cardiac Operative Risk Evaluation (EuroSCORE) is an another method of calculating predicted mortality for patients undergoing cardiac surgery (EuroSCORE 2014). In the PARTNER trials, both the STS and EuroSCORE were reported. Since then, the EuroSCORE has been superseded by the EuroSCOREII in 2011. The EuroSCORE II requires the following information:

1. Patient-related factors: Age, gender, renal impairment, extracardiac arteriopathy, poor mobility, previous cardiac surgery, chronic lung disease, active endocarditis, critical preoperative state, diabetes on insulin;
1. Cardiac related factors: NYHA, CCS class 4 angina, LV function, recent myocardial infarction (within 90 days), pulmonary hypertension;
2. Operation related factors: urgency (elective, urgent, emergency or salvage), weight of the intervention, surgery on thoracic aorta.

Studies have found that the EuroSCORE overestimates risk and that the STS risk score performs better. The table below presents the review of some studies that assessed the relevance of using a STS or EuroSCORE in vascular diseases.

Table 11 - Studies that assessed the STS and EuroSCORE frameworks

Study	Sample size	Intervention	Conclusion
(Le Tourneau, Pellikka et al. 2010)	674	Surgical management (n=160) or medical management (n=514)	STS is a relevant tool for predicting long-term outcome and for selecting patients who benefit markedly from early surgery. It predicts long-term survival irrespective of the strategy.
(Wendt, Osswald et al. 2009)	652	Isolated AVR	Euroscore overestimates mortality. STS is more suitable in assessing perioperative mortality.
(Ad, Barnett et al. 2007)	3,125	Coronary artery bypass	STS risk score performs better than the EuroSCORE in predicting operative mortality. STS risk score provides risk estimates much closer to actual observed rates while the EuroSCORE provides individual mortality estimates exceeding the STS estimates and the actual observed estimates. The study found that the overall mortality rate was 1.8%, 2.9% for female patients and 1.5% for males. The predicted overall STS mortality was 2.6%, and 4.1% and 2.1% for female and male patients. The predicted overall EuroSCORE mortality was 5.2%, and 7.9% and 4.5% for female and male patients respectively.
(Basraon, Chandrashekhar et al. 2011)	537	AVR	The EuroSCORE substantially overestimates perioperative mortality risk. The observed operative mortality rate in the whole cohort was 5.9%. The mortality predicted by the EuroSCORE and the STS score were 15.6% and 3.6% respectively.
(Parolari, Pesce et al. 2010)	26,621 (meta-analysis)	Valve surgery	The EuroSCORE overpredicts risk. Alternative risk scoring system should be considered.

Appendix 2

Articles of interest for TAVI

1. Elmariah S, et al. Outcomes of transcatheter and surgical aortic valve replacement in high-risk patients with aortic stenosis and left ventricular dysfunction: results from the Placement of Aortic Transcatheter Valves (PARTNER) trial (cohort A). Circ Cardiovasc Interv. 2013, 6(6):604-14.

2. Barbanti M, et al. Impact of preoperative moderate/severe mitral regurgitation on 2-year outcome after transcatheter and surgical aortic valve replacement: insight from the Placement of Aortic Transcatheter Valve (PARTNER) Trial Cohort A. Circulation. 2013, 128(25):2776-84.

3. Green P, et al. Relation between six-minute walk test performance and outcomes after transcatheter aortic valve implantation (from the PARTNER trial). Am J Cardiol. 2013, 112(5):700-6.

4. Makkar RR, et al. Determinants and outcomes of acute transcatheter valve-in-valve therapy or embolization: a study of multiple valve implants in the U.S. PARTNER trial (Placement of AoRTic TraNscathetER Valve Trial Edwards SAPIEN Transcatheter Heart Valve). J Am Coll Cardiol. 2013, 62(5):418-30.

5. Herrmann HC, et al. Predictors of mortality and outcomes of therapy in low-flow severe aortic stenosis: a Placement of Aortic Transcatheter Valves (PARTNER) trial analysis. Circulation. 2013, 127(23):2316-26.

6. Hahn RT, et al. Comparison of transcatheter and surgical aortic valve replacement in severe aortic stenosis: a longitudinal study of echocardiography parameters in cohort A of the PARTNER trial (placement of aortic transcatheter valves). J Am Coll Cardiol. 2013, 61(25):2514-21.

7. Reynolds MR, et al. Cost-effectiveness of transcatheter aortic valve replacement compared with surgical aortic valve replacement in high-risk patients with severe aortic stenosis: results of the PARTNER (Placement of Aortic Transcatheter Valves) trial (Cohort A). J Am Coll Cardiol. 2012, 60(25):2683-92.

8. Green P, et al. The impact of frailty status on survival after transcatheter aortic valve replacement in older adults with severe aortic stenosis: a single-center experience. JACC Cardiovasc Interv. 2012, 5(9):974-81.

9. Reynolds MR, et al. Health-related quality of life after transcatheter or surgical aortic valve replacement in high-risk patients with severe aortic stenosis: results from the PARTNER (Placement of AoRTic TraNscathetER Valve) Trial (Cohort A). J Am Coll Cardiol. 2012;60(6):548-58.

10. Kodali SK, et al. Two-year outcomes after transcatheter or surgical aortic-valve replacement. N Engl J Med. 2012; 366(18):1686-95.

11. Makkar RR, et al. Transcatheter aortic-valve replacement for inoperable severe aortic stenosis. N Engl J Med. 2012; 366(18):1696-704.

12. Miller DC, et al. Transcatheter (TAVR) versus surgical (AVR) aortic valve replacement: occurrence, hazard, risk factors, and consequences of neurologic events in the PARTNER trial. J Thorac Cardiovasc Surg. 2012; 143(4):832-843.e13.

13. Reynolds MR, et al. Health-related quality of life after transcatheter aortic valve replacement in inoperable patients with severe aortic stenosis. Circulation. 2011; 124(18):1964-72.

14. Smith CR, et al. Transcatheter versus surgical aortic-valve replacement in high-risk patients. N Engl J Med. 2011; 364(23):2187-98.

15. Leon MB, et al. Transcatheter aortic-valve implantation for aortic stenosis in patients who cannot undergo surgery. N Engl J Med. 2010; 363(17):1597-607.

APPENDIX 3

ANZ TAVI Platforms Summary

Product Name	Company	First in Man Completed	CE Mark Approval	FDA Approval	TGA Approval	Valve Design
SAPIEN – TF	EL	April 2002	Sept 2007	Nov 2011	Sept 2013	Balloon Expanded Stainless Steel Frame
CoreValve - TF	Med	July 2004	May 2007	Jan 2014	-	Self- Expanding Nitinol
SAPIEN – TA	EL	Nov 2005	Sept 2007	Oct 2012	Sept 2013	Balloon Expanded Stainless Steel Frame
SAPIEN XT – TF	EL	2008	March 2010	June 2014	-	Balloon Expanded Cobalt Chromium Frame
SAPIEN XT – TA / Tao	EL	2008	March 2010	June 2014	-	Balloon Expanded Cobalt Chromium Frame
SAPIEN 3 – TF	EL	2009	Jan 2014	-	-	Balloon Expanded Cobalt Chromium Frame
SAPIEN 3 – TA / Tao	EL	2009	Jan 2014	-	-	Balloon Expanded Cobalt Chromium Frame
Lotus	BS	2010	Oct 2013	-	-	Self- Expanding Nitinol
PORTICO – TF	StJ	June 2011	Nov 2012	-	-	Self- Expanding Nitinol
PORTICO – TA	StJ	Nov 2012	-	-	-	Self- Expanding Nitinol
Corevalve Evolut R	Med	Sept 2013	-	-	-	Self- Expanding Nitinol

EL = Edwards Lifesciences; BS = Boston Scientific; StJ = St Jude Medical; Med = Medtronic; TF = transfemoral; TA = trans-apical; Tao = trans-aortic

Source: https://www.cvpipeline.com

Medtronic - Corevalve

Overview Description

System consists of a multi-level, self-expanding, nitinol frame; a self-manufactured porcine pericardial tissue valve; a sheathed delivery catheter; and a loading system; this profile also covers a new "profile adaptive sheath"

History

A timeline of key events includes the following, according to a presentation at TVT on June 8, 2010 by Jean-Claude Laborde, MD:

- The first CoreValve transcatheter AVR by the antegrade approach was performed by Dr. Jean-Claude Laborde et al. on July 12, 2004
- The first CoreValve percutaneous AVR by retrograde approach was Oct. 12, 2006 by Drs. Patrick Serruys, Pieter de Jaegere, and Jean-Claude Laborde
- The first CoreValve AVR by axillary approach was performed on June 30, 2006 by Drs. Laborde et al.
- The first CoreValve AVR by transaortic approach was performed in Nov. 2008 by Dr. Bleiziffer et al.
- The first CoreValve AVR by carotid approach was performed on Oct. 19, 2009 by Drs. Modine et al.

On May 16, 2007, CoreValve announced that it has received the CE Mark for the ReValving System with the 18 Fr delivery system to treat high-risk patients.

On Feb. 23, 2009, Medtronic announced it has signed a definitive agreement to acquire CoreValve in a deal calling for an initial payment of $700 million plus additional payments contingent upon the achievement of agreed milestones. Medtronic said its manufacturing and global distribution strengths will “accelerate” the use of CoreValve’s technology.

On April 9, 2009, Medtronic announced that it completed the acquisition of CoreValve.

In a presentation at TCT on Sept. 21, 2009, Jeffrey Popma, MD, said that Medtronic is seeking the following indication for use for the CoreValve ReValving system:

- Indicated for use in patients with aortic stenosis necessitating valve replacement who are considered poor surgical candidates with high surgical risk (STS score greater than or equal to 8 and/or elevated peri-operative mortality risk of greater than or equal to 15%)

On Aug. 18, 2011, Medtronic announced CE Mark approval for the 31 mm CoreValve.

On Nov. 2, 2011, Medtronic announced that it received approval from the Korea Food & Drug Administration for the CoreValve System in Oct. 2011.

On May 23, 2013, Medtronic announced CE Mark approval for valve-in-valve (VIV) procedures using CoreValve and CoreValve Evolut in 3 delivery approaches (transfemoral, subclavian and direct aortic access). All 4 sizes are also approved for valve-in-valve procedures (23, 26, 29, and 31 mm).

U.S. ROLLOUT PLANS:

In a presentation at TCT on Oct. 31, 2013, Medtronic said that its commercial site selection process will include

- Site registration required via an online web site that will document key site information
- Center selection and queuing criteria:
  - Meets NCD requirements and procedure volumes
  • Functioning heart teams and admin support
  • Strength of valve clinic
- Training and education: A 5-step process that focuses on the implant heart team and the extended support team:
  - Online modules, which provide background online training for primary extended support team; curriculum will focus on aortic anatomy/aortic stenosis, patient imaging and selection, product and procedure
  - Product and procedure training, with a 1-day didactic session for the primary implant team; curriculum will focus on device information (IFU), imaging and patient selection, procedural steps and taped case, hands-on simulation, complication management, and post-procedure care
  - Heart team training, which involves on-site in-service for extended heart team; this includes a final review for site readiness (includes patient selection, procedural team prep, checklist review, surgical back-up plan, device loading, anesthesia planning, intra-operative echo review, post-op patient management, and inventory management plan)
  - Supported cases, which involves an expert CoreValve instructor being present at 5 to 10 cases (their role is to ensure best practices and evaluate readiness of sites to operate independently) as well as ongoing case support from Medtronic's therapy specialist personnel and imaging/patient selection support
  - Continuing education and surveillance, which includes training resources for ongoing case support and imaging services, a training and education committee, field complaint handling, and post-approval outcomes data collection (TVT National Registry)

On Jan. 17, 2014, Medtronic announced that it has received FDA approval of CoreValve for severe aortic stenosis patients who are too ill or frail to have their aortic valves replaced through traditional open-heart surgery. The FDA approved the entire CoreValve platform, including the CoreValve Evolut 23 mm, and the CoreValve 26, 29, and 31 mm valves.

In a March 29, 2014 press release, Medtronic said that upon reviewing the CoreValve IDE trial's results for high-risk patients (presented at ACC on March 29, 2014), the FDA determined it has sufficient information to evaluate the safety and efficacy of the CoreValve System for this patient group without the need for an external expert panel.

On April 11, 2014, Edwards reported that the U.S. District Court for the District of Delaware granted on that day a preliminary injunction limiting the sale of Medtronic's CoreValve system in the U.S., with the injunction scheduled to go into effect in 7 business days. At the conclusion of the hearing, Chief Judge Gregory Sleet ordered Edwards and Medtronic to confer on what instances the CoreValve device could continue to be used in the treatment of U.S. patients at centers currently trained on CoreValve. Medtronic indicated in an April 11, 2014 press release that it will appeal the federal district court ruling.

Source: https://www.cvpipeline.com

Edwards - SAPIEN TF

Overview Description

Edwards SAPIEN THV is a stainless steel, balloon-expandable support structure (stent) with an integrated, uni-directional trileaflet tissue valve now made of bovine) and treated with Edwards' ThermaFix™ advanced tissue process) and a PET fabric cuff; this profile covers transfemoral delivery

History

This product is based on the work of H. Andersen et al., and is the result of Edwards' acquisition of Percutaneous Valve Technologies (PVT) in January 2004 for $125 million in cash plus up to an additional $30 million in payments based on achieving key milestones through 2007. Two of PVT's founders were Martin Leon, MD, president and chief executive officer of the Cardiovascular Research Foundation (New York, NY) and Alain Cribier, MD, chief of Cardiology of University Hospital (Rouen, France). At the time of the purchase, the PVT aortic heart valve was in use in compassionate cases in Europe. Edwards initially planned to seek a Humanitarian Device Exemption in the U.S. in parallel with an IDE and a PMA, but in a January 2005 analyst's call, the company announced it would focus solely on the IDE/PMA regulatory path.

In Q3 2005, Edwards completed the transition of valve manufacturing capability from 3F Therapeutics, and received FDA approval for Edwards as a manufacturing site. As part of this, Edwards recorded a special charge of $22.8 million related to the restructuring of development and supply agreements between 3F and PVT, which had been established before Edwards purchased PVT in early 2004. Under the terms of the agreements, Edwards paid $23 million in cash, with an additional payment of $2 million to be paid under certain conditions. Edwards is currently producing percutaneous valves in Irvine, CA, according to the company's 10K, filed March 10, 2006.

Edwards originally called this product the Cribier-Edwards Aortic Bioprosthesis-Model 900. During its Dec. 8, 2006 investor conference, Edwards announced that the next-generation product is known as the Edwards-SAPIEN THV.

On Sept. 5, 2007, Edwards announced that it received the CE Mark for the Edwards SAPIEN THV with the RetroFlex transfemoral delivery system. In a presentation at EuroPCR on May 15, 2008, Martyn Thomas, MD, described the CE Mark indication as follows:

- Patients with symptomatic aortic stenosis (aortic valve area less than 0.8 cm2) requiring aortic valve replacement who are at high risk for operative mortality
- Or patients who are "non-operable" as determined by 1 of the following risk assessments: Logistic EuroScore of greater than 20% or STS score of greater than 10

On May 12, 2008, Edwards said that it will introduce RetroFlex II, its next-generation transfemoral delivery system for the Edwards SAPIEN THV, at EuroPCR 2008. RetroFlex II adds a tapered nose cone designed to facilitate the passage of the valve delivery catheter over

the curve of the aortic arch and through the diseased aortic heart valve, according to the May 12, 2008 press release.

On Feb. 11, 2009, Edwards announced CE Mark approval of the RetroFlex III transfemoral delivery system.

During a presentation at Credit Suisse on Nov. 11, 2010, Edwards said that it has submitted the PARTNER-Cohort B PMA to the FDA.

On June 7, 2011, Edwards announced that the FDA panel meeting for use of Edwards SAPIEN THV in inoperable patients will be held on July 20, 2011. The company is seeking the following indications for use:
The Edwards SAPIEN Transcatheter Heart Valve, model 9000TFX, sizes 23mm and 26mm, and RetroFlex 3 Delivery System are indicated for transfemoral delivery in patients with severe aortic stenosis who have been determined by a cardiac surgeon to be inoperable for open aortic valve replacement and in whom existing co-morbidities would not preclude the expected benefit from correction of the aortic stenosis.

On July 20, 2011, the FDA's circulatory system devices panel recommended approval of Edwards SAPIEN THV for the treatment of certain inoperable patients. The panel noted that the proposed indications for use statement was generally acceptable for this specific patient population (Cohort B) who are not candidates for open surgical aortic valve replacement, with the following additions to the existing language:

- The word "symptomatic" should added to the indications statement to adequately describe the patients in the trial
- There should be a specific mention that the device can be implanted in a patient's native valve as a way to address the lack of available data regarding valve-in-valve implantation technique

Other issues that were addressed in the FDA panel meeting on July 20, 2011 included:

- Labeling should include warnings that there is no data supporting valve-in-valve use
- The patient brochure should include explicit definitions of "neurological event" vs. "stroke"
- Modifications to labeling should be made so that physicians and patients are clearly aware of potential neurological adverse event risks with use of the device
- A standardized anti-coagulation/antiplatelet protocol should be implemented for all Edwards SAPIEN THV patients and Edwards should revisit over time whether or not any changes should be made to this protocol
- Edwards SAPIEN THV training program for new practitioners proposed by Edwards, which includes a minimum number of proctored procedures, biweekly procedure meetings, and centers of excellence, is a good starting point
- Patient selection should be strict and that new enrollment sites should be critiqued closely; a phased enrollment model should be used to avoid enrolling 75 sites at once
- Stroke risk needs to be examined closely in the post-market setting
- Hemodynamic performance of Edwards SAPIEN THV should be monitored in Edwards' post-approval study to verify durability

- QoL data on Edwards SAPIEN THV should be collected in both proposed post-approval studies (the PARTNER Cohort B extended scope study and the 2nd post-approval study) through 5 years of follow-up
- Data should be collected in the form of a post-market registry for all valve-in-valve use of Edwards SAPIEN THV, if it occurs after device approval

On Nov. 2, 2011, Edwards announced FDA approval of the transfemoral delivery of the Edwards SAPIEN transcatheter aortic heart valve for the treatment of inoperable patients with severe symptomatic aortic stenosis. The Edwards SAPIEN valve is indicated for transfemoral delivery in patients with severe symptomatic native aortic valve stenosis who have been determined by a cardiac surgeon to be inoperable for open aortic valve replacement and in whom existing co-morbidities would not preclude the expected benefit from correction of the aortic stenosis.

On April 9, 2012, Edwards announced that the FDA panel meeting for use of Edwards SAPIEN THV in high-risk patients is June 13, 2012. On June 13, 2012, the FDA's circulatory system devices panel voted to recommend approval of Edwards SAPIEN transcatheter heart valve via transfemoral and transapical delivery for high-risk patients with severe, symptomatic aortic stenosis; the vote was 11 to 0, with 1 abstention, that benefits outweighed risks.

On Oct. 19, 2012, Edwards announced that FDA has approved its SAPIEN transcatheter aortic heart valve delivered both transfemorally and transapically for high-risk aortic stenosis.

During its Q3 2013 earnings call on Oct. 28, 2013, Edwards said that it has received approval for SAPIEN in Australia.

Source: https://www.cvpipeline.com

Edwards - SAPIEN TA

Overview Description

Transapical delivery system for Edwards SAPIEN THV, a stainless steel, balloon-expandable support structure (stent) with an integrated, uni-directional trileaflet tissue valve now made of bovine) and treated with Edwards' ThermaFix™ advanced tissue process) and a PET fabric cuff

History

Edwards developed the procedure for use with the Ascendra system in partnership with surgical teams led by Michael Mack, MD (Medical City, Dallas), Friedrich Mohr, MD, PhD (Leipzig, Germany), and Gerhardt Wimmer-Greinecker, MD, of Frankfurt, Germany.

Edwards has said that the first TAP procedure was performed in Nov. 2005 by John Webb, MD (an interventional cardiologist who is an investigator with the percutaneous system), and Samuel Lichtenstein, MD (a cardiothoracic surgeon), at St. Paul's Hospital in Vancouver.

At the STS/AATS Tech-Con meeting on Jan. 29, 2006, Gerhardt Wimmer-Greinecker, MD, of Frankfurt, Germany, presented the first human cases, all performed OUS. All 4 of the first

implantations resulted in explantations, and 3 had “unacceptable” paravalvular leaks. He added that the solution the investigators subsequently discovered was “dramatic oversizing” using a 26 mm sized valve (the first 4 implants were done with a 23 mm valve). As of the date of the presentation, another 4 patients had been implanted using the oversizing technique; all 4 were successful and there was only 1 case of paravalvular leak.

On Sept. 5, 2007, Edwards announced that it submitted for CE Mark approval of the Edwards SAPIEN THV with the Ascendra transapical delivery system, and that approval is expected by the end of 2007. During its investor conference on Dec. 7, 2007, Edwards said that it received CE Mark approval for Ascendra on Dec. 6, 2007. The product was launched in Europe in Q1 2008.

During its earnings call for Q2 2011 on July 21, 2011, Edwards said that in April 2011, it submitted its PMA for PARTNER-Cohort A.

On April 9, 2012, Edwards announced that the FDA panel meeting for use of Edwards SAPIEN THV in high-risk patients is June 13, 2012. On June 13, 2012, the FDA’s circulatory system devices panel voted to recommend approval of Edwards SAPIEN transcatheter heart valve via transfemoral and transapical delivery for high-risk patients with severe, symptomatic aortic stenosis; the vote was 11 to 0, with 1 abstention, that benefits outweighed risks.

On Oct. 19, 2012, Edwards announced that FDA has approved its SAPIEN transcatheter aortic heart valve delivered both transfemorally and transapically for high-risk aortic stenosis.

On Sept. 23, 2013, the FDA announced it has approved revised labeling for the Edwards SAPIEN THV, making the device available to an expanded group of patients who have inoperable aortic valve stenosis. The new labeling removes references to specific access points now making it available for inoperable patients who need an alternate access point (other than transfemoral or transapical). The revised labeling was based on Edwards’ submission of Transcatheter Valve Therapy Registry (TVTR) in the U.S. and THV device registries in Europe, along with data from FDA-approved clinical studies and peer-reviewed medical journals.

During its Q3 2013 earnings call on Oct. 28, 2013, Edwards said that it has received approval for SAPIEN in Australia.

Source: https://www.cvpipeline.com

Edwards - SAPIEN XT TF

Overview Description

Next-generation transcatheter heart valve (made of bovine pericardial tissue treated with ThermaFix anti-calcification process) with a transfemoral delivery system (18 Fr), enhanced durability, and “unsurpassed” hemodynamics"; has a cobalt-chromium frame

History

Edwards first discussed publicly this next-generation transcatheter heart valve on its Q2 2007 earnings call on July 23, 2007. The company stated during the call that it expects the first clinical use of this new valve in 2008, and added that this valve will require its own clinical trial and cannot be approved simply through a PMA supplement.

On March 2, 2010, Edwards announced CE Mark approval of the SAPIEN XT transcatheter aortic heart valve with the NovaFlex transfemoral delivery system.

On its Q1 2011 earnings call on April 20, 2011, Edwards said that at EuroPCR in May 2011, it will introduce both its expandable sheath (“eSheath”), designed to reduce vascular complications, and the NovaFlex Plus delivery system, which it says is designed for ease of use and has ergonomic enhancements.

On May 20, 2011, Edwards announced it has received CE Mark approval for sale in the European Union of the NovaFlex+ transfemoral delivery system. The company reported it was launching this system, as well as the eSheath expandable sheath technology, at EuroPCR 2011.

On June 6, 2011, Edwards announced the successful first Chinese implants of the Edwards SAPIEN XT valve. The transfemoral valve implantations were performed in May as special access cases at the Second Military Medical University, under a joint educational and training program on transcatheter aortic valve implantation between the university and Edwards.

In an interview with cvPipeline on June 1, 2012, Edwards said that it has issued a Field Safety Notice for certain model and serial numbers of its surgical and transcatheter heart valves that were packaged at its manufacturing facility in Horw, Switzerland, and distributed to Europe, Asia, Canada, Africa, Latin America, Australia and Japan. The U.S. is not impacted by this notice. This action is being taken because the company found that, in some cases, the valve jar may contain 1 or more extremely small particles that were unintentionally introduced during the packaging process. The company said that it believes the risk of injury is highly unlikely for patients already implanted with an affected device. Edwards has identified and corrected the cause related to this Field Safety Notice and notified customers and the relevant regulatory authorities. Appx. 1,000 surgical heart valves and 50 transcatheter heart valves are involved. The FDA is not involved, the company said in its June 1, 2012 interview with cvPipeline.

During its Q2 2012 earnings call on July 24, 2012, Edwards indicated that it received CE Mark approval of the 29 mm valve in Europe in the middle of Q2 2012.

On June 24, 2013, Edwards announced that it has received approval of Edwards SAPIEN XT in Japan. The company said it expects to obtain reimbursement approval from MHLW by year's end, and will initiate a full launch in Japan immediately thereafter.

During a presentation at Bank of America on May 15, 2013, Edwards said that it submitted its PMA for PARTNER II-Cohort B at the end of April 2013.

On Aug. 21, 2013, Edwards announced that Japan's Central Social Insurance Medical Council (Chuikyo) has approved the recommendation by the Japanese Ministry of Health, Labor and Welfare's (MHLW) expert review panel to provide reimbursement forEdwards SAPIEN XT. The reimbursement is scheduled to go into effect on Oct. 1, 2013, according to the Aug. 21, 2013 press release. With this approval, Chuikyo established a reimbursement of 4.53 million yen (appx. $46,000 at current exchange rates) for when SAPIEN XT valve is used in the treatment of patients with severe symptomatic aortic stenosis. The reimbursement rate for medical devices in Japan covers the cost of the device as well as taxes, certain hospital fees, and distribution expenses.

During its Q3 2013 earnings call on Oct. 28, 2013, Edwards said that it has received approval for SAPIEN XT in Canada.

On Feb. 5, 2014, Edwards announced it has received CE Mark approval in Europe for aortic and mitral valve-in-valve procedures using the SAPIEN XT valve in patients at extreme risk for surgery.

Source: https://www.cvpipeline.com

Edwards - SAPIEN XT TA/Tao

Overview Description

2nd-gen, lower-profile version of Ascendra transapical delivery system for use with the Edwards SAPIEN XT; Ascendra+ is designed for both transapical and transaortic approaches; available for 23, 26, and 29 mm

History

Edwards first discussed publicly a transapical version of its next-generation transcatheter heart valve on its Q1 2009 earnings call on April 27, 2009.

In a Sept. 8, 2009 press release, Edwards said that its Ascendra 2 system is the "result of direct surgeon feedback and close clinical partnership" that has resulted in "meaningful refinements" to the system and procedure.

On March 2, 2010, Edwards announced CE Mark approval of the SAPIEN XT transcatheter aortic heart vale with the Ascendra 2 transapical delivery system.

On Feb. 24, 2011, Edwards announced CE Mark approval of the 29 mm version of Edwards SAPIEN XT, available with the Ascendra transapical delivery system.

In an interview with cvPipeline on June 1, 2012, Edwards said that it has issued a Field Safety Notice for certain model and serial numbers of its surgical and transcatheter heart valves that were packaged at its manufacturing facility in Horw, Switzerland, and distributed to Europe, Asia, Canada, Africa, Latin America, Australia and Japan. The U.S. is not impacted by this notice. This action is being taken because the company found that, in some cases, the valve jar may contain 1 or more extremely small particles that were unintentionally introduced during the packaging process. The company said that it believes the risk of injury is highly unlikely for patients already implanted with an affected device. Edwards has identified and corrected the cause related to this Field Safety Notice and notified customers and the relevant regulatory authorities. Appx. 1,000 surgical heart valves and 50 transcatheter heart valves are involved. The FDA is not involved, the company said in its June 1, 2012 interview with cvPipeline.

During its Q2 2012 earnings call, Edwards said that late in Q2 2012, it received CE Mark approval of Ascendra Plus for both transapical and transaortic approaches.

On June 24, 2013, Edwards announced that it has received approval of Edwards SAPIEN XT in Japan. The company said it expects to obtain reimbursement approval from MHLW by year's end, and will initiate a full launch in Japan immediately thereafter.

On Aug. 21, 2013, Edwards announced that Japan's Central Social Insurance Medical Council (Chuikyo) has approved the recommendation by the Japanese Ministry of Health, Labor and Welfare's (MHLW) expert review panel to provide reimbursement forEdwards SAPIEN XT. The reimbursement is scheduled to go into effect on Oct. 1, 2013, according to the Aug. 21, 2013 press release. With this approval, Chuikyo established a reimbursement of 4.53 million yen (appx. $46,000 at current exchange rates) for when SAPIEN XT valve is used in the treatment of patients with severe symptomatic aortic stenosis. The reimbursement rate for medical devices in Japan covers the cost of the device as well as taxes, certain hospital fees, and distribution expenses.

During its Q3 2013 earnings call on Oct. 28, 2013, Edwards said that it has received approval for SAPIEN XT in Canada.

On Feb. 5, 2014, Edwards announced it has received CE Mark approval in Europe for aortic and mitral valve-in-valve procedures using the SAPIEN XT valve in patients at extreme risk for surgery.

Source: https://www.cvpipeline.com

Edwards - SAPIEN 3 TF

Overview Description

Next-generation balloon-expandable transcatheter heart valve delivered through a 14 Fr expandable eSheath; features a paravalvular leak solution and improved distal flexing

History

Edwards first discussed publicly its work on this project during its analyst day on Dec. 10, 2009. Edwards said during its Dec. 10, 2009 analyst day that it is working on enhanced transcatheter heart valve designs below 18 Fr.

In a clinicaltrials.gov posting for the company's CE Mark trial dated March 7, 2013, Edwards indicated that Edwards SAPIEN 3 is indicated for use in symptomatic patients (intermediate or higher operable risk) with severe aortic stenosis requiring aortic valve replacement.

On Jan. 13, 2014, Edwards announced completion of enrollment of its U.S. clinical trial studying the SAPIEN 3 valve in the treatment of high-risk or inoperable patients.

On Jan. 27, 2014, Edwards announced that it has received CE Mark approval of the SAPIEN 3 valve and has initiated its launch.

During its Q4 2013 earnings call on Feb. 4, 2014, Edwards said that it has commenced "an aggressive" launch of this device in Europe, with a number of successful implants already in 2014. The company noted that upgrading customers to this new platform "should be fast" as there is no need for extensive training and clinicians are "very eager" to get their hands on this exciting new technology. The company added that "for these reasons, we believe SAPIEN 3 will quickly become the leading transcatheter valve in Europe."

Source: https://www.cvpipeline.com

Edwards - SAPIEN 3 TA / Tao

Overview Description

Next-generation balloon-expandable transcatheter heart valve designed for both transapical and transaortic approaches; features the Certitude delivery system

History

In a clinicaltrials.gov posting for the company's CE Mark trial dated March 7, 2013, Edwards indicated that Edwards SAPIEN 3 is indicated for use in symptomatic patients (intermediate or higher operable risk) with severe aortic stenosis requiring aortic valve replacement.

On Jan. 13, 2014, Edwards announced completion of enrollment of its U.S. clinical trial studying the SAPIEN 3 valve in the treatment of high-risk or inoperable patients.

On Jan. 27, 2014, Edwards announced that it has received CE Mark approval of the SAPIEN 3 valve and has initiated its launch. In an interview with cvPipeline on Feb. 5, 2014, the company said that the approval is for the 23, 26, and 29 mm valves.

During its Q4 2013 earnings call on Feb. 4, 2014, Edwards said that it has commenced "an aggressive" launch of this device in Europe, with a number of successful implants already in 2014. The company noted that upgrading customers to this new platform "should be fast" as there is no need for extensive training and clinicians are "very eager" to get their hands on this exciting new technology. The company added that "for these reasons, we believe SAPIEN 3 will quickly become the leading transcatheter valve in Europe."

Source: https://www.cvpipeline.com

Medtronic - Evolut R

Overview Description

Next generation of CoreValve technology designed for enhanced annular seal (to minimize paravlavular leak) and reduced conduction disturbances; lower profile improves patient access and reduces major vascular complications; can be resheathed and retrieved based on positioning

History

The first-in-man procedure was performed at McGill on Sept. 16, 2013 using the 23 mm CoreValve Evolut R.

On Oct. 22, 2013, Medtronic announced that it has initiated a clinical study of the new recapturable CoreValve Evolut R delivery system.

Source: https://www.cvpipeline.com

Boston - Lotus

Overview Description

Low-profile, customized, self-expanding, pre-loaded percutaneous aortic valve prosthesis featuring a continuous elongated nitinol wire braid with a suspended bovine pericardial trileaflet valve; redesigned version has 18 Fr delivery system

History

One of Sadra's founders was Donald Baim, MD.

On Nov. 19, 2010, Boston Scientific announced the signing of a definitive merger agreement, under which it will acquire Sadra. The agreement calls for an upfront payment of $225 million plus additional potential payments of up to $225 million upon achievement of specified regulatory and revenue-based milestones through 2016. At the time of the announcement, Boston Scientific already owned 14% of Sadra, meaning the actual upfront cash payment will be $193 million plus additional potential milestone payments up to $193 million. Boston Scientific had been an investor in Sadra since 2006.

Other investors in Sadra besides Boston Scientific included Accuitive Medical Ventures, Finistere, Firstmark Capital, HealthCor Partners, Incept LLC, Oakwood, ONSET Ventures, and SV Life Sciences.

On Jan. 4, 2010, Boston Scientific announced that it has completed its acquisition of Sadra Medical.

Speaking at TVT on June 6, 2011, Eberhard Grube, MD, said that the 27 mm design of the valve has been finalized. In a presentation at TVT on June 7, 2011, Ian Meredith, MD, said that the 27 mm valve has achieved 200 million cycles in testing.

In a presentation at Stifel Nicolaus Weisel Healthcare Conference on Sept. 11, 2013, Boston Scientific said that it has filed for CE Mark approval of the Lotus valve.

On Oct. 28, 2013, Boston Scientific announced CE Mark approval of the Lotus valve.

Source: https://www.cvpipeline.com

St Jude - PORTICO TF

Overview Description

Transfemoral aortic valve replacement system featuring a self-expanding stent design; features 18 Fr delivery system; built on the Trifecta valve platform

History

St. Jude first announced this program during its annual investor meeting on Feb. 6, 2009. The company reported that it began to focus on this program during 2008 after it became comfortable that the opportunity was becoming "real enough"; at the same time, the company decided to shift its level of investment from PFO closure devices after that opportunity did not meet expectations to the transcatheter aortic valve program.

On June 7, 2011, St. Jude said this product is called Portico. At a presentation at TVT on June 6, 2011, Gregory Fontana, MD, said the first-in-man case with the transfemoral delivery system was performed in Vancouver on June 3, 2011.

On Nov. 19, 2012, St. Jude announced CE Mark approval of the 23 mm Portico THV and transfemoral delivery system.

On Dec. 12, 2013, St. Jude announced CE Mark approval of the 25 mm Portico THV.

During its analyst day on Feb. 7, 2014, St. Jude said that its 23 and 25 mm valves are market released and being commercialized via a CE Mark. The next 2 sizes, 27 and 29 mm, are expected to be commercialized in the 2nd half of 2014.

St Jude - PORTICO TA

Overview Description

Transapical aortic valve replacement system featuring a self-expanding stent design with bovine pericardium; transapical delivery system does not require an external sheath for apical access

History

St. Jude first announced this program during its annual investor meeting on Feb. 6, 2009. The company reported that it began to focus on this program during 2008 after it became comfortable that the opportunity was becoming “real enough”; at the same time, the company decided to shift its level of investment from PFO closure devices after that opportunity did not meet expectations to the transcatheter aortic valve program.

In June 7, 2011, St. Jude said this product is called Portico.

On Nov. 15, 2012, John Webb, MD, et al. performed the first human case with Portico TA.

Source: https://www.cvpipeline.com

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