Australian Government

Department of Health

Application Form

(New and Amended

Requests for Public Funding)

(Version 2.4)

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires in order to determine whether a proposed medical service is suitable.

Please use this template, along with the associated Application Form Guidelines to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted.

Should you require any further assistance, departmental staff are available through the Health Technology Assessment Team (HTA Team) on the contact numbers and email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

Phone: +61 2 6289 7550
Fax: +61 2 6289 5540
Email: hta@health.gov.au
Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant): Edwards Lifesciences Pty Ltd
Corporation name:
ABN: 77 098 873
Business trading name: Edwards Lifesciences Pty Ltd

Primary contact name:

REDACTED

Alternative contact name:

REDACTED

2. (a) Are you a lobbyist acting on behalf of an Applicant?

☐ Yes
☒ No

(b) If yes, are you listed on the Register of Lobbyists?

☐ Yes
☒ No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

3. Application title

Transcatheter aortic valve implantation (TAVI) via transfemoral delivery using the SAPIEN 3 balloon-expandable valve (BEV) system for patients at intermediate risk for surgery.

4. Provide a succinct description of the medical condition relevant to the proposed service (no more than 150 words – further information will be requested at Part F of the Application Form)

Severe aortic stenosis (AS) is characterised by narrowing of the aortic valve leading to restriction of blood flow. AS is often caused by a build-up of calcium on the valve leaflets, causing them to become stiff and reducing their ability to open and close efficiently. It is associated with high pressure inside the left ventricle and as a result of the excessive workload, the left ventricle hypertrophies, which further leads to inefficiency in blood circulation. Symptoms include angina, dyspnoea and syncope. Left untreated, heart failure develops, and the risk of death is increased.

This application is relevant to patients with severe, symptomatic AS classified as being at *intermediate risk* of surgery. Intermediate risk is historically defined by a predicted 30-day risk of surgical mortality of 4-8%, based on the Society of Thoracic Surgeons Predicted Risk of Mortality (STS-PROM) score.

5. Provide a succinct description of the proposed medical service (no more than 150 words – further information will be requested at Part 6 of the Application Form)

TAVI involving the SAPIEN 3 BEV involves minimally invasive transfemoral insertion of a prosthetic heart valve that is positioned within the native aortic annulus using the SAPIEN 3 system. Once in situ, the valve is expanded while the heart is rapidly paced. The procedure is performed using fluoroscopic and transoesophageal guidance and under general or local anaesthesia.

6. (a) Is this a request for MBS funding?

☒ Yes
☐ No

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

☐ Amendment to existing MBS item(s)
☒ New MBS item(s)

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service:

Not applicable.

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

Not applicable.

i. ☐ An amendment to the way the service is clinically delivered under the existing item(s)
ii. ☐ An amendment to the patient population under the existing item(s)
iii. ☐ An amendment to the schedule fee of the existing item(s)
iv. ☐ An amendment to the time and complexity of an existing item(s)
v. ☐ Access to an existing item(s) by a different health practitioner group
vi. ☐ Minor amendments to the item descriptor that does not affect how the service is delivered
vii. ☐ An amendment to an existing specific single consultation item
viii. ☐ An amendment to an existing global consultation item(s)
ix. ☐ Other (please describe below):

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

i. ☐ A new item which also seeks to allow access to the MBS for a specific health practitioner group
ii. ☒ A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)
iii. ☐ A new item for a specific single consultation item
iv. ☐ A new item for a global consultation item(s)

NB: There is an existing MBS item number (38495) for TAVIs: "TAVI, for the treatment of symptomatic severe aortic stenosis, performed via transfemoral delivery, unless transfemoral delivery is contraindicated or not feasible, in a TAVI Hospital on a TAVI Patient by a TAVI Practitioner – includes all intraoperative diagnostic imaging that the TAVI Practitioner performs upon the TAVI Patient". However, as per note TN.8.135, the item is currently restricted to patients who have been "assessed as having an unacceptably high risk for surgical aortic valve replacement". The current proposal seeks a new MBS item for the *TAVI with the SAPIEN 3 BEV* system, and for patients at *intermediate* risk for surgery.

(f) Is the proposed service seeking public funding other than the MBS?

☐ Yes
☒ No

(g) If yes, please advise:

7. What is the type of service:

☒ Therapeutic medical service
☐ Investigative medical service
☐ Single consultation medical service
☐ Global consultation medical service
☐ Allied health service
☐ Co-dependent technology
☐ Hybrid health technology

8. For investigative services, advise the specific purpose of performing the service *(which could be one or more of the following)*:

i. ☐ To be used as a screening tool in asymptomatic populations
ii. ☐ Assists in establishing a diagnosis in symptomatic patients
iii. ☐ Provides information about prognosis
iv. ☐ Identifies a patient as suitable for therapy by predicting a variation in the effect of the therapy
v. ☐ Monitors a patient over time to assess treatment response and guide subsequent treatment decisions

9. Does your service rely on another medical product to achieve or to enhance its intended effect?

☐ Pharmaceutical / Biological
☒ Prosthesis or device
☐ No

10. (a) If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

Not applicable

☐ Yes
☐ No

(b) If yes, please list the relevant PBS item code(s):

Not applicable

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

Not applicable

☐ Yes (please provide PBAC submission item number below)
☐ No

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical?

Not Applicable

11. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List?

☒ Yes
☐ No

(b) If yes, please provide the following information (where relevant):

Billing code(s): EL063
Trade name of prosthesis: Edwards SAPIEN 3 Transcatheter Heart Valve.
Clinical name of prosthesis: Transcatheter, balloon expanded aortic heart valve with Commander Delivery System.
Other device components delivered as part of the service: The prostheses listing includes the valve and delivery system.

(c) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

Not Applicable

☐ Yes
☐ No

(d) Are there any other sponsor(s) and / or manufacturer(s) that have a similar prosthesis or device component in the Australian market place which this application is relevant to?

☐ Yes
☒ No
NB: Other TAVI devices (St Jude Medical and Medtronic) do not involve balloon-expandable valves. Rather, they involve self-expanding valves, which are currently *not* TGA-approved for intermediate risk patients.

(e) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s):

12. Please identify any single and / or multi-use consumables delivered as part of the service?

Single use consumables: angioplasty kit which includes drapes, manifolds and extensions tubing.
Small and large bore vascular access sheaths
Lock syringes
3 way taps x 2
3 x bowls
2 x galley pots
Temporary pacing wire
Variety of pre-shaped catheters
Variety of standard or speciality wires
Multi-use consumables: temporary pacing cable, temporary pacing box and transthoracic or transoesophageal probe

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

13. (a) If the proposed medical service involves the use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer or any other type of therapeutic good, please provide the following details:

Type of therapeutic good: transfemoral - aortic transcatheter heart valve bioprosthesis, stent-like framework.
Manufacturer's name: Edwards Lifesciences LLC.
Sponsor's name: Edwards Lifesciences Pty Ltd.

(b) Is the medical device classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?

☒ Class III
☐ AIMD
☐ N/A

14. (a) Is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

☐ Yes (If yes, please provide supporting documentation as an attachment to this application form)
☒ No

(b) If no, has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?

☒ Yes (if yes, please provide details below)
☐ No

ARTG listing, registration or inclusion number: 284496

TGA approved indication(s), if applicable: "The Edwards SAPIEN 3 valve, Edwards delivery system, and accessories are indicated for use in patients with severe, symptomatic, calcific aortic valve stenosis who are judged by a Heart Team to be at intermediate or greater risk for open surgical therapy (i.e., predicted risk of surgical mortality; greater than or equal to 3% at 30 days, based on the Society of Thoracic Surgeons (STS) risk score and other clinical comorbidities unmeasured by the STS risk calculator)."

NB: Older-generation TAVI *SAPIEN XT* BEVs (ARTG IDs 250696 and 250697) are also listed on the ARTG, but Edwards Lifesciences Corporation no longer markets these in Australia, and they are *not* part of the present application. Compared to the SAPIEN XT BEVs, the SAPIEN 3 BEV system has a better profile and more precise handling and positioning, which reduces the risk of post-procedural paravalvular aortic leak.

TGA approved purpose(s), if applicable: As above.

15. If the therapeutic good has not been listed, registered or included in the ARTG, is the therapeutic good in the process of being considered for inclusion by the TGA?

Not applicable
☐ Yes (please provide details below)
☐ No

16. If the therapeutic good is not in the process of being considered for listing, registration or inclusion by the TGA, is an application to the TGA being prepared?

Not applicable
☐ Yes (please provide details below)
☐ No

PART 4 – SUMMARY OF EVIDENCE

17. **Provide an overview of all key journal articles or research published in the public domain related to the proposed service that is for your application (limiting these to the English language only).** ***Please do not attach full text articles, this is just intended to be a summary.***

	Type of study design*	**Title of journal article or research project (including any trial identifier or study lead if relevant)**	**Short description of research (max 50 words)****	**Website link to journal article or research (if available)**	**Date of publication*****
1.	Single-arm clinical trial, with comparative analyses based on propensity score analysis	Thourani VH, et al. 'Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: propensity score analysis' Lancet. 2016; 387 (10034): p.2218-25	Single-arm clinical trial (PARTNER S3i) of 1078 intermediate risk patients with severe AS who underwent TAVI with the SAPIEN 3 BEV, with comparison against a cohort of 1021 patients who underwent surgical aortic valve replacement (SAVR) in the PARTNER 2A randomised clinical trial (of TAVI SAPIEN XT BEV with SAVR). Comparisons were made using propensity score analysis. SAPIEN 3 TAVI BEV was superior to SAVR with respect to the primary composite endpoint of mortality, strokes, and moderate or severe aortic regurgitation(-9.2%, 95%CI [-13.0;-5.4], p<0.0001).	https://www.ncbi.nlm.nih.gov/pubmed/27053442	May 2016
2.	Single-arm clinical trial, with comparative analyses based on propensity score matching	Baron SJ, et al. 'Effect of SAPIEN 3 Transcatheter Valve Implantation on Health Status in Patients With Severe Aortic Stenosis at Intermediate Surgical Risk: Results From the PARTNER S3i Trial.' JACC Cardiovasc Interv. 2018; 11(12): 1188-1198.	Sub-study of PARTNER S3i. 1068 intermediate risk patients with severe AS who underwent TAVI with the SAPIEN 3 BEV, were compared against a cohort of 936 patients who underwent SAVR in PARTNER 2A. Comparisons were made using propensity score analysis. Quality of life (QoL) was assessed using the Kansas City Cardiomyopathy Questionnaire (KCCQ) instrument. SAPIEN 3 TAVI BEV was associated with improved KCCQ score at one month (diff=15.6, p<0.001) and one year (2.0, p<0.05) versus SAVR.	www.ncbi.nlm.nih.gov/pubmed/29860075	June 2018

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
3.	Cohort study	Kodali S, et al. 'Early clinical and echocardiographic outcomes after SAPIEN 3 transcatheter aortic valve replacement in inoperable, high-risk and intermediate-risk patients with aortic stenosis.' Eur Heart J. 2016; 37: 2252–2262.	Patients with severe, symptomatic AS (high risk or inoperable N=583, intermediate risk N=1078) underwent TAVI with the SAPIEN 3 BEV. The transfemoral route was used in 86.9% of patients, and the transapical or transaortic route in 13.1%. Among intermediate risk patients, 30-day all-cause mortality was 1.1%. Frequency of other outcomes were as follows: major/disabling stroke 1.0%, major bleeding 10.6%, major vascular complications 6.1%, and permanent pacemaker 10.1%.	https://www.ncbi.nlm.nih.gov/pubmed/27190101	July 2016
4.	Cohort study	Tham JLM, et al. 'Clinical outcomes of self-expanding vs. balloon-expandable TAVI for severe aortic stenosis.' Acta Cardiol. 2019 1:1-8.	151 patients undergoing TAVI, comprising 46.3% with self-expanding valves and 53.6% with balloon-expandable valves (SAPIEN 3 and older generation SAPIEN XT). This real-world retrospective analysis demonstrated higher rates of moderate or greater paravalvular regurgitation (6.7 vs. 0.0%; p=0.02), stroke (12.4 vs. 1.4%; p=0 .04) and pacemaker insertion (36.4 vs. 9.5%; p=0.001) with self-expanding compared to balloon-expandable valves at 30 day post-TAVI.	https://doi.org/10.1080/00015385.2019.1572959	January 2019
5.	Cost-effectiveness analysis	Zhou J, et al. 'Cost-effectiveness of transcatheter aortic valve implantation compared to surgical aortic valve replacement in the intermediate surgical risk population.' Int J Cardiol. 2019. pii: S0167-5273(19)30985-4.	Costs and outcomes of TAVI BEV and SAVR in intermediate risk patients were compared using a Markov model. Efficacy and cost inputs were derived from the PARTNER S3i study and published sources. TAVI was dominant over SAVR: costs were $10,000 less, with 0.33 more life years and 0.31 more QALYs lived.	https://www.ncbi.nlm.nih.gov/pubmed/31255453	June 2019

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
6.	Cost-effectiveness analysis	Baron S.J. 'Cost-effectiveness of transcatheter vs. surgical aortic valve replacement in intermediate risk patients. Results from the PARTNER 2A and SAPIEN 3 intermediate risk trials.'	Decision analysis comparing costs and outcomes among intermediate risk patients undergoing TAVI and SAVR. Data inputs from published studies.	www.ncbi.nlm.nih.gov/pubmed/30586747	February 2019

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment, including providing the trial registration number to allow for tracking purposes.*

**** If the publication is a follow-up to an initial publication, please advise.*

18. Identify yet to be published research that may have results available in the near future that could be relevant in the consideration of your application by MSAC (limiting these to the English language only). *Please do not attach full text articles, this is just intended to be a summary.*

Not applicable

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

19. **List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the service (please attach a statement of clinical relevance from each group nominated):**

    Cardiac Society of Australia and New Zealand (CSANZ)

20. **List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service):**

    Australian and New Zealand Society of Cardiac and Thoracic Surgeons

    Cardiac Society of Australia and New Zealand (CSANZ)

21. **List the relevant consumer organisations relevant to the proposed medical service (please attach a letter of support for each consumer organisation nominated):**

    Consumer Health Forum

22. **List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service:**

23. **Nominate two experts who could be approached about the proposed medical service and the current clinical management of the service(s):**

    Name of expert 1: redacted

    Telephone number(s): redacted

    Email address: redacted

    Justification of expertise: redacted

    Name of expert 2: redacted

    Telephone number(s): redacted

    Email address: redacted

    Justification of expertise: redacted

    Please note that the Department may also consult with other referrers, proceduralists and disease specialists to obtain their insight.

PART 6 – POPULATION (AND PRIOR TESTS), INDICATION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

24. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease in terms of both morbidity and mortality:

Aortic stenosis (AS) is one of the most common and serious valve diseases. It is characterised by a narrowing of the aortic valve opening, which restricts blood flow from the left ventricle to the aorta and causes pressure build-up in the left ventricle and consequent left ventricular hypertrophy. Furthermore, stenotic aortic valves may not close fully, resulting in regurgitation back into the left ventricle.

The most common cause of AS is age-related calcification of the aortic valve. Less common causes are congenital bicuspid aortic valves and rheumatic heart disease. Other than calcification, the pathophysiological features of AS are inflammation, lipid accumulation and subendothelial thickening.[1]

AS is a progressive disease that is asymptomatic until late stages. Symptomatic severe AS is classified as Stage D AS, and has the following features: symptoms (see below); calcified valve leaflets with reduced opening; jet velocity (V_{max}) ≥4 m/s; and mean gradient ≥40 mm Hg. Variations in valve haemodynamics and the presence of symptoms are used to further subclassify symptomatic severe AS.[2] Symptoms of AS include exertional dyspnoea, decreased exercise tolerance, exertional angina and exertional syncope or presyncope. Left untreated, patients will progress to heart failure.[2] Patients are then at high risk for sudden death. Prognosis is poor once there is a mean aortic valve gradient greater than 40mmHg. Severe AS is associated with death rates of 38%, 32% and 18% at one, five years and ten years, respectively[3]. Without aortic valve replacement, the survival of these patients can be as low as 50% at two years and 20% at five years.[4]

This application is relevant to patients with severe, symptomatic AS classified as being at intermediate risk of surgery. Intermediate risk is historically defined by predicted risk of surgical mortality of 4-8% at 30 days, based on the STS-PROM score.

25. Specify any characteristics of patients with the medical condition, or suspected of, who are proposed to be eligible for the proposed medical service, including any details of how a patient would be investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the service:

Patients with severe AS are typically elderly, although those with a congenital malformation of the valve may present earlier. Patients may present with symptoms or be diagnosed incidentally. Regardless of presentation, an echocardiograph is needed to confirm the diagnosis of AS. Echocardiographic criteria for *severe* AS are as follows.[5]

Valve area (cm^2)	**<1.0**
Indexed valve area (cm^2/m^2 body surface area)	**<0.6**

[1] Thaden J.J. et al *'The Global Burden of Aortic Stenosis'* Prog. CardVasc. Dis 56 (2014) 565-571
[2] Nishamura R A., et al *'2014 AHA/ACC Guideline for the Management of Patients with Valvular Heart Disease: Executive Summary.' JACC Vol 63, Iss 22, 2014*
[3] Varadarajan P et al *'Clinical profile and natural history of 453 nonsurgically managed patients with severe aortic stenosis'* Ann Thorac Surg. 2006 Dec; 82(6):2111-5
[4] Otto CM. Timing of aortic valve surgery. *Heart*. 2000;84:211-8.
[5] Andeotti F et al *'Guidelines on the management of valvular heart disease (version 2012): The Joint Task Force on the Management of Valvular Heart Disease of the European Society of Cardiology (ESD) and the European Association for Cardio-Thoracic Surgery (EACTS)* Eur Heart Journ Vol 33, Iss 19, 1 Oct 2012

Valve area (cm^2)	**<1.0**
Mean gradient (mmHg)	**>40.0**
Maximum jet velocity (m/s)	**>4.0**
Velocity ratio	**<0.25**

Other investigations that may be conducted include cardiac magnetic resonance imaging (MRI), exercise echocardiography, multi-slice computed tomography and coronary angiography. Valvular regurgitation is also assessed. Functional status is assessed by the New York Heart Association (NYHA) functional class system.

Assessment of surgical risk is determined by a multi-disciplinary 'heart team'. This application pertains to patients who are determined to be at intermediate risk of surgery by a heart team.[6] Intermediate risk is defined by predicted risk of surgical mortality of 4-8% at 30 days, based on the STS-PROM score.

26. Define and summarise the current clinical management pathway *before* patients would be eligible for the proposed medical service (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway up to this point):

At present, patients with severe symptomatic AS at intermediate risk of surgery are managed medically and/or undergo surgical aortic valve replacement (SAVR). Medical management consists of pharmacological treatment to alleviate symptoms. These do not alter the disease course nor improve survival. Some patients undergo balloon aortic valvuloplasty to enlarge the aortic valve opening, but this procedure also does not alter the disease course nor survival.

PART 6b – INFORMATION ABOUT THE INTERVENTION

27. Describe the key components and clinical steps involved in delivering the proposed medical service:

In Australia, TAVI is performed in a cardiac catheterisation or an operating room. TAVI is performed under general anaesthesia or local anaesthesia with sedation. For transfemoral delivery (relevant to this application), the latter is often sufficient. The procedure is performed without cardio-pulmonary bypass.

TAVI is usually performed under the guidance of fluoroscopy and transoesophageal echocardiography (TOE). Aortography may also be used. A percutaneous sheath is inserted into the femoral artery with a guide wire that is pushed passed the aortic valve. The aortic valve is predilated via balloon valvuloplasty while the heart is rapidly paced. The SAPIEN 3 BEV is mounted on a balloon catheter and is inserted percutaneously over the guidewire until it crosses the aortic valve. Optimum positioning is confirmed by fluoroscopy. Once the correct position is confirmed, the heart is again rapidly paced and the balloon is expanded until the device meets the native annular walls. The balloon is then deflated and the catheter and guidewire are removed.

Immediately following the procedure, aortography and TOE are again performed to assess the location and the degree of any aortic regurgitation, and the functioning of the coronary arteries.

Patients are then transferred for monitoring to either a coronary care, high dependency or intensive care unit.

28. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

SAPIEN 3 is a registered trademark of Edwards Lifesciences Corporation or its affiliates. Edwards Lifesciences Corporation has ceased marketing of the older generation SAPIEN XT BEV (ARTG IDs 250696

[6] Kodali S et al *'Early clinical and echocardiographic outcomes after SAPIEN 3 transcatheter aortic valve replacement inoperable, high-risk and intermediate -risk patients with aortic stenosis'* Eur Heart Journ doi:10.1093/eurheartj/ehw112

and 250697) in Australia, and these are *not* part of the present application. There are other TAVI valves available in Australia, but these valves are self-expanding rather than balloon-expandable, so do not employ a balloon catheter. Current data suggest that balloon-expandable valves are associated with better outcomes compared to self-expanding valves.[7] [8]

29. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

TAVI using the SAPIEN 3 BEV system is currently included on the MBS for patients with symptomatic severe aortic stenosis who are at *high risk* for surgery or who are inoperable. TAVI using the SAPIEN 3 BEV represents a new approach in Australia for treating patients who have symptomatic severe aortic stenosis who are at intermediate risk for surgery. Only balloon-expandable valves (SAPIEN 3 and SAPIEN XT) are currently TGA-approved for use in intermediate risk patients.

30. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency):

It is anticipated that in nearly all cases, TAVI using the SAPIEN 3 BEV system would be delivered only once in a patient's lifetime.

31. If applicable, identify any healthcare resources or other medical services that would need to be delivered <u>at the same time</u> as the proposed medical service:

It is not anticipated that additional resources or medical services would be delivered at the same time, other than those that would occur during the TAVI.

32. If applicable, advise which health professionals will primarily deliver the proposed service:

An interventional cardiologist or a cardiothoracic surgeon must perform the procedure.

33. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery:

The service cannot be delegated.

34. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it:

MBS funding is only available for cardiothoracic surgeons or interventional cardiologists who are accredited TAVI practitioners.

35. If applicable, advise what type of training or qualifications would be required to perform the proposed service as well as any accreditation requirements to support service delivery:

Cardiothoracic surgeons must have completed the Cardiothoracic Surgery Program and be eligible to be a Fellow of the Royal Australasian College of Surgeons, or otherwise qualified to practice cardiothoracic surgery in Australia.

Interventional cardiologists must have completed the Advanced Training Curriculum in Cardiology and be eligible to be a Fellow of the Royal Australasian College of Physicians or otherwise qualified to practice interventional cardiology in Australia.

Additionally, the interventional cardiologist or cardiothoracic surgeon must be an accredited TAVI practitioner. Accreditation is conducted by the Accreditation Committee appointed by Cardiac Accreditation Services Limited[9]

[7] Noorani et al *'Differences in Outcomes and Indications between SAPIEN and CoreValve Transcatheter Aortic Valve'* Interv Card Rev Vol 9 Issue 2 2014

[8] Wijeysundera H.C. *'Comparison of Outcomes of Balloon-Expandable Versus Self-Expandable Transcatheter Heart Valves foe Severe Aortic Stenosis'* Am J Cardiol 2017; 119: 1094-1099

[9] http://tavi.org.au/

36. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select all relevant settings):

- ☒ Inpatient private hospital
- ☒ Inpatient public hospital
- ☐ Outpatient clinic
- ☐ Emergency Department
- ☐ Consulting rooms
- ☐ Day surgery centre
- ☐ Residential aged care facility
- ☐ Patient's home
- ☐ Laboratory
- ☐ Other – please specify below

The service must be provided in a hospital that has been endorsed for undertaking TAVIs. Accreditation is conducted by the Accreditation Committee appointed by Cardiac Accreditation Services Limited[10]

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each:

The service may be provided in either a public or private hospital, as long as it is endorsed (see above).

37. Is the proposed medical service intended to be entirely rendered in Australia?

- ☒ Yes
- ☐ No – please specify below

[10] http://tavi.org.au/

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

38. Nominate the appropriate comparator(s) for the proposed medical service, i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system (including identifying health care resources that are needed to be delivered at the same time as the comparator service):

The comparator is SAVR with a bioprosthetic or mechanical aortic valve. As with TAVI with the SAPIEN 3 BEV, it is not anticipated that other resources would be required at the same time other than those that are provided during the SAVR procedure.

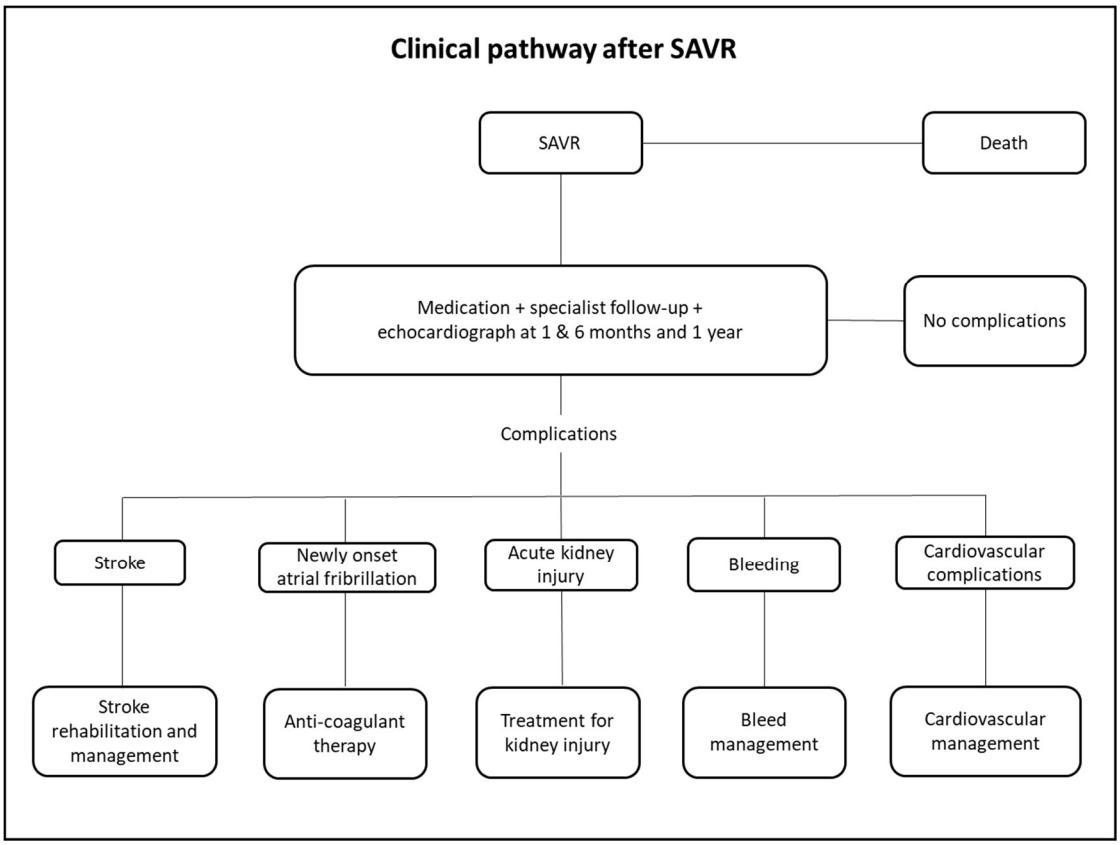
39. Does the medical service that has been nominated as the comparator have an existing MBS item number(s)?

☒ Yes (please provide all relevant MBS item numbers below)
☐ No

38488 **VALVE REPLACEMENT with BIOPROSTHESIS OR MECHANICAL PROSTHESIS** **Fee: $1,909.60**
38489 **VALVE REPLACEMENT with allograft (subcoronary or cylindrical implant), or unstented xenograft** **Fee: $2,271.05**

40. Define and summarise the current clinical management pathways that patients may follow *after* they receive the medical service that has been nominated as the comparator (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway that patients may follow from the point of receiving the comparator onwards including health care resources):

Patients receiving SAVR receive an echocardiogram at one month, six months and one year after the procedure. Complications of SAVR include stroke, heart failure, permanent pacemaker implantation, and other cardiovascular events. Re-operation may be needed, but this is rare. See the attached 'Clinical Pathway after SAVR'.



41. (a) Will the proposed medical service be used in addition to, or instead of, the nominated comparator(s)?

It will be *instead of* the nominated comparator.

☐ Yes
☐ No

(b) If yes, please outline the extent of which the current service/comparator is expected to be substituted:

It is estimated that as many as 80 percent of intermediate risk patients may access TAVI BEV, should the service be included on the MBS. Please see responses to Questions 49 and 50 for further information.

42. Define and summarise how current clinical management pathways (from the point of service delivery onwards) are expected to change as a consequence of introducing the proposed medical service including variation in health care resources (Refer to Question 39 as baseline):

The clinical pathway will be the same after TAVI with the SAPIEN 3 BEV as for SAVR, but the likelihood of outcomes will differ. Efficacy data suggest that survival at one year is higher for TAVI with the SAPIEN 3 BEV (92.6% vs 87.0%) and major stroke is lower (2.3% vs 5.9%). However, pacemaker implantation is higher (12.4% vs 9.4%)[11]. It should also be noted that SAVR requires open chest surgery, and hence typically involves a longer hospital stay, including in the intensive care unit (ICU) or high dependency unit compared to TAVI BEV. Recovery time is also likely to be longer with SAVR.

[11] Thourani VH et al *'Transcatheter aortic valve replacement versus surgical valve replacement in intermediate-risk patients: a propensity score analysis'* The Lancet April 3, http://dx.doi.org/10.1016/S0140-6736(16)30073-3

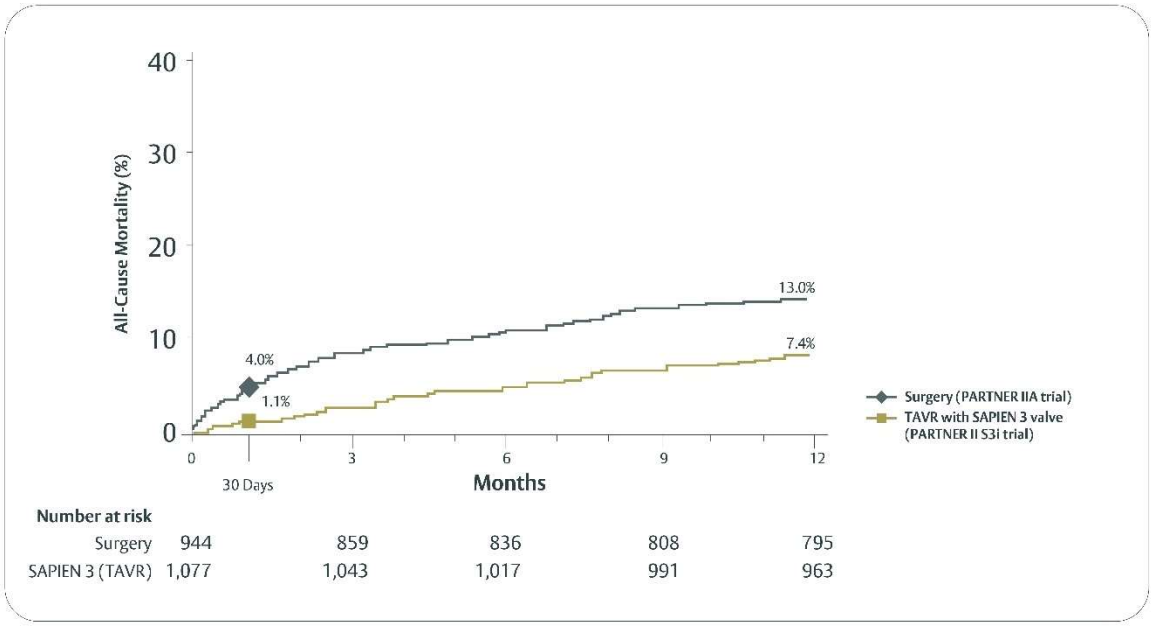
PART 6d – INFORMATION ABOUT THE CLINICAL OUTCOME

43. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms):

TAVI with the SAPIEN 3 BEV is superior to SAVR in patients with symptomatic severe AS and at intermediate risk of surgery in terms of overall survival and the incidence of disabling stroke. TAVI with the SAPIEN 3 BEV also results in significantly lower rates for new onset atrial fibrillation (AF), major bleeding events and acute kidney injury.

Overall survival:

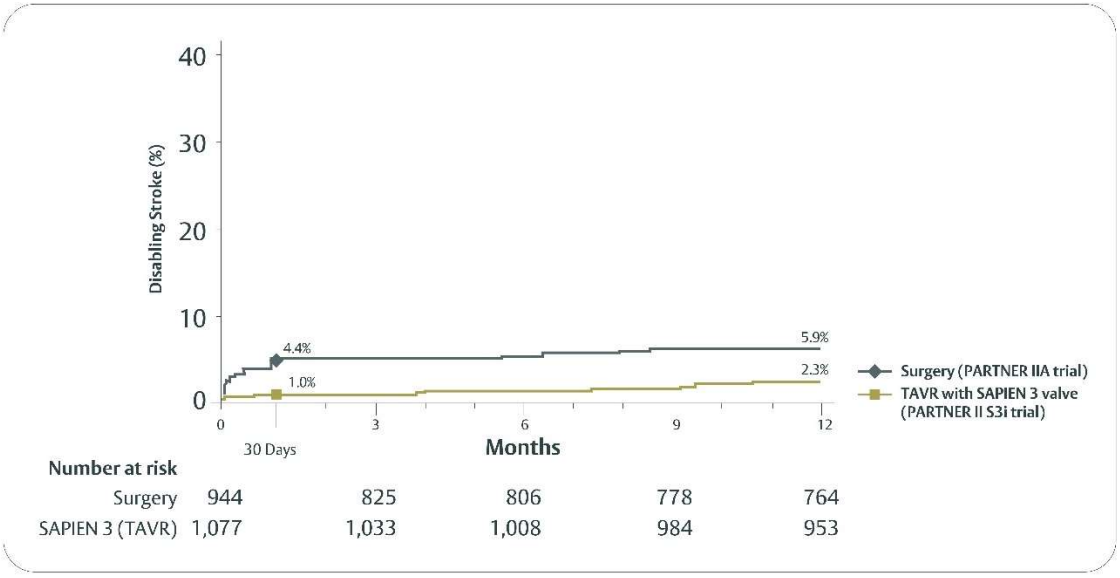
In the single-arm PARTNER S3i trial, 1078 intermediate risk patients with severe AS were implanted with the SAPIEN 3 valve. Outcomes over two years were compared with those of 1021 patients randomised to SAVR in the PARTNER 2A trial using propensity score analysis. (PARTNER 2A was a randomised controlled trial of TAVR BEV using the older generation SAPIEN XT valve versus SAVR in intermediate risk patients with severe AS.) PARTNER S3i and PARTNER 2A recruited the same profile of patients. Survival rates were significantly higher for TAVI using the SAPIEN 3 BEV among patients in PARTNER S3i compared to SAVR patients in PARTNER 2A (see figure below).



Disabling stroke:

In the PARTNER S3i propensity score analysis, the rate of major/disabling stroke with TAVI using the SAPIEN 3 BEV was lower than that with SAVR.

	Rates of major/disabling stroke	
	30 days	1 year
PARTNER S3i Propensity Score Analysis		
TAVI using the SAPIEN 3 BEV	1.0%	2.3%
SAVR (from PARTNER 2A)	4.4%	5.9%



New onset atrial fribrillation (AF):

In the PARTNER S3i propensity score analysis, rates of new-onset AF were lower with TAVI using the SAPIEN 3 BEV than SAVR at both 30 days and one year.

	Rates of new-onset atrial fibrillation	
	30 days	1 year
PARTNER S3i propensity score analysis		
TAVI using the SAPIEN 3 BEV	5.0%	5.9%
SAVR (from PARTNER 2A)	28.3%	29.2%

Cardiac death:

The rate of cardiac death was higher for SAVR in the the PARTNER 2A trial both at 30 days and one year when compared to TAVI using the SAPIEN 3 BEV in the PARTNER S3i propsensity score analysis.

	Rates of cardiac death	
	30 days	1 year
PARTNER S3i propensity score analysis		
TAVI using the SAPIEN 3 BEV	0.9%	4.5%
SAVR (from PARTNER 2A)	3.1%	8.1%

Major bleeding events:

The PARTNER S3i propensity score analysis showed that the 30-day rate of life-threatening or disabling bleeding was considerably lower with TAVI using the SAPIEN 3 BEV than SAVR.

	Rates of major bleeding events
	30 days
PARTNER S3i propensity score analysis	
TAVI using the SAPIEN 3 BEV	4.6%[a]
SAVR (from PARTNER 2A)	46.7%[a]
[a] Major bleeding not reported; rates for life-threatening or disabling bleeding.	

Acute kidney injury:

In the PARTNER 2 S3i propensity score analysis, the 30-day rate of acute kidney injury was lower with TAVI using the SAPIEN 3 BEV than SAVR.

	Rates of acute kidney injury
	30 days
PARTNER S3i propensity score analysis [a]	
TAVI using the SAPIEN 3 BEV	0.5%
SAVR (from PARTNER 2A)	3.3%
[a] Stage 3.	

Major vascular complications:

The 30-day rate of major vascular complications was slightly higher for TAVI using the SAPIEN 3 BEV based on the PARTNER S3i propensity score analysis compared to SAVR.

	Rates of major vascular complications
	30 days
PARTNER S3i propensity score analysis	
TAVI using the SAPIEN 3 BEV	6.1%
SAVR (from PARTNER 2A)	5.4%

Myocardial infarction:

The rate of myocardial infarction was higher for SAVR in the PARTNER 2A trial both at 30 days and one year compared to TAVI using the SAPIEN 3 BEV in the PARTNER S3i propensity score analysis.

	Rates of myocardial infarction	
	30 days	1 year
PARTNER S3i propensity score analysis		
TAVI using the SAPIEN 3 BEV	0.3%	0.3%
SAVR (from PARTNER 2A)	1.9%	3.1%

44. Please advise if the overall clinical claim is for:

☒ Superiority
☐ Non-inferiority

45. Below, list the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be specifically measured in assessing the clinical claim of the proposed medical service versus the comparator:

Safety Outcomes:

Major stroke

New onset atrial fibrillation

Major bleeding events

Myocardial infarction

Other major vascular complications

Acute kidney injury

Clinical Effectiveness Outcomes:

Overall survival

Health-related quality of life

Healthcare resources

Cost of valvular prosthesis

Cost associated with changes in clinical management (testing required before the procedure, length of stay, post-discharge rehabilitation)

Cost-effectiveness:

Cost per life-year gained

Cost per QALY gained

Total Australian Government healthcare costs:

Total cost to the Medical Benefits Schedule (MBS)

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

46. Estimate the prevalence and/or incidence of the proposed population:

Osnabrugge estimated that 3.4% of the population aged over 75 years have severe AS. Of those, 75.6% would be symptomatic. It is estimated that 15.8% of patients with severe symptomatic AS are at intermediate risk of surgery.[12] Thourani et al [13] estimated from the STS data set that 13.9% of patients who underwent SAVR were of intermediate risk.

It was assumed that the same prevalence of severe AS (3.4%) would apply to people aged 65 years and above as those aged 75 years and above. The following table lists the estimated Australian population aged 65 years and above.

Australian population over 65 years[14]

	2018	2019	2020
Australian Population over 65 years of age	**3,909,104**	**4,026,056**	**4,145,275**

An estimate of the number of patients who would be eligible for the proposed service can be made from the number of MBS item numbers that have been claimed for SAVR procedures. TAVI became available on the MBS in November 2017. This is likely to have reduced the overall population that received SAVR since this date. Therefore, Medicare statistics prior to November 2017 were accessed to avoid underestimating the population.

In the year from Quarter 4 2016 to Quarter 3 2017, MBS Item 38488 was claimed 2601 times and MBS Item 38489 was claimed 90 times. Eighty percent of these patients were aged over 65 years and likely to be eligible for TAVI.[15]

According to Australian Institute of Health and Welfare statistics[16], 1827 patients received TAVI in Australia in 2017/2018. It is possible that some of these patients would have been treated in private hospitals should the option have been available. To avoid underestimation of the population, it was assumed that all these patients would have been treated in the private sector if TAVI had been available.

The following estimates are made using the utilisation of MBS item numbers 38488 and 38489 as a proportion of the population aged 65 years and over. The same methodology is applied to TAVI procedures. Only 80% of patients receiving SAVR under these item numbers are for those aged 65 and over, so this is likely to be a conservative estimate.

[12] Osnabrugge MS et al *'Aortic Stenosis in the Elderly. Disease Prevalence and Number of Candidates for Transcatheter Aortic Valve Replacement: A Meta-Analysis and Modelling Study'* JACC 2013 Vol. 62, No 11, 2013

[13] Thourani VH et al *'Contemporary real-world outcomes of surgical aortic valve replacement in 141,905 low-risk, intermediate-risk, and high-risk patients.'* Ann Thorac Surg 2015;99:55-61

[14] Australian Bureau of Statistics Population Projections Australia 2017. Series B

[15] http://medicarestatistics.humanservices.gov.au/statistics/mbs_item.jsp

[16] Australian Institute of Health and Welfare, Procedures and healthcare interventions (ACHI 9th edition), Australia, 2017-18

		2017	2018	2019	2020	20201
A	Australian Population over 65 years of age	3,790,665	3,909,104	4,026,056	4,145,275	4,271,505
B	MBS item numbers 38488 and 38489	2691	2775	2858	2943	3032
C	TAVI Procedures	1827	1884	1940	1998	2059
D	Total AVR population (B+C)	4518	4659	4799	4941	5091
C	Intermediate Risk Group (15.8% of D)	714	736	758	781	804

47. Estimate the number of times the proposed medical service(s) would be delivered to a patient per year:

As this intervention is usually performed late in life, it is anticipated that the service would only be delivered once per patient.

48. How many years would the proposed medical service(s) be required for the patient?

Once in a lifetime.

49. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year:

It is estimated that 804 patients would be eligible for the proposed service in 2021. However, it is unlikely that all these patients would access TAVI. At present, referral to a 'heart team' is not routine. Therefore, if a patient is referred to a cardiologist or a surgeon who is not part of a heart team, the patient may not be given the option of receiving TAVI. This figure is therefore likely to be an overestimate.

Osnabrugge estimated that 80% of high risk/inoperable patients eligible for TAVI received the procedure. If this figure is applied to intermediate risk patients who are eligible, then in 2021, 644 patients would receive TAVI using the SAPIEN 3 BEV.

50. Estimate the anticipated uptake of the proposed medical service over the next three years factoring in any constraints in the health system in meeting the needs of the proposed population (such as supply and demand factors) as well as provide commentary on risk of 'leakage' to populations not targeted by the service:

A TAVI must be performed by a TAVI practitioner in a 'TAVI-endorsed' hospital. It is possible that there will be capacity constraints if there are insufficient facilities and trained medical staff to meet demand. It is likely that capacity will increase in coming years. However, assuming that capacity is available to meet demand, the following uptake is likely.

		2022	2023	2024
A	**Australian Population over 65 years of age**	**4,397,463**	**4,526,677**	**4,656,293**
B	**Eligible Population**	**828**	**852**	**877**
C	**Patients accessing TAVI** **80% X B**	**662**	**682**	**701**

As access to TAVI is determined by the TAVI heart team, it is unlikely that there will be leakage to populations outside the eligible population.

PART 8 – COST INFORMATION

51. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown:

redacted

Other cost items include the following MBS items

Cost Item	MBS Item Number	100% MBS Fee	75% Benefit
TAVI Case Conference -Organiser	**6080**	**$50.15**	**$37.65**
TAVI Case Conference Attendance X 3	**6081**	**$37.40**	**$28.05**
TAVI Procedure including all intraoperative diagnostic imaging	**XXXX**	**$1,432.20 (Same as MBS item 38495)**	**$1,074**
Assistant	**51303**	**$286.40**	**$214.80**
Initiation of Anaesthesia	**21941**	**$138.60**	**$103.95**
Anaesthesia Time Units 1:41 to 1:45 hours	**23073**	**$138.60**	**$103.95**
ICU Attendance	**13870**	**$362.10**	**$271.60**
Transthoracic echocardiography	**55113**	**$230.65**	**$173.00**

52. Specify how long the proposed medical service typically takes to perform:

The procedure typically takes 1 to 1.5 hours.

53. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and medical service usage characteristics that would define eligibility for MBS funding.

Category 3 – Therapeutic Procedures – Surgical Operations
TAVI using the SAPIEN 3 balloon-expandable valve system, for the treatment of symptomatic severe aortic stenosis, performed via transfemoral delivery, unless transfemoral delivery is contraindicated or not feasible, in a TAVI Hospital on a TAVI Patient by a TAVI Practitioner – includes all intraoperative diagnostic imaging that the TAVI Practitioner performs upon the TAVI Patient

NB: The same explanatory notes (AN.33.1 and TN.8.135) for MBS item 38495 would apply for the new MBS item, except that the description of the 'TAVI Patient' would be changed to: "A TAVI Patient means a patient who, as a result of a TAVI Case Conference, has been assessed as having an ~~unacceptably high~~ intermediate risk for surgical aortic valve replacement and is recommended as being suitable to receive the service described in item XXXX."