Population

Describe the population in which the proposed health technology is intended to be used:

The proposed population are patients with moderate to severe, or severe, symptomatic degenerative (primary) mitral valve regurgitation.

Specify any characteristics of patients with the medical condition, or suspected of, who are proposed to be eligible for the proposed health technology, describing 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 technology:

Patients with moderate-severe or severe MR are determined by echocardiography and objective and subjective measures (i.e. MR grading of 3+ [moderate-severe] or 4+ [severe]) and who are symptomatic (NYHA functional class II or greater). Patient selection should be performed by a multi-disciplinary heart team (MDHT) specialising in the treatment of mitral regurgitation to assess patient risk and anatomical suitability.

A patient will generally be referred by a general practitioner to a cardiologist if the presence of MR is suspected, who in turn refers the patient to either an interventional cardiologist or a cardiothoracic surgeon.

The first step after MR has been detected is to perform an assessment of the anatomy to determine the mechanism of regurgitation, FMR or DMR. In DMR there is leaflet abnormally whereas in FMR there is ventricular remodelling (Table 1) (Zhogbi et al 2017).

Table 1. Etiology of Primary and Secondary MR

Disease	Presentation	Result
Primary MR (leaflet abnormality)	Mitral valve prolapse myxomatous changes	Prolapse, flail, ruptured or elongated chordae
	Degenerative changes	Calcification, thickening
	Infectious	Endocarditis vegetations, perforations, aneurysm
	Inflammatory	Rheumatic, collagen vascular disease, radiation, drugs
	Congenital	Cleft leaflet, parachute mitral valve
Secondary MR (ventricular remodeling)	Ischemic etiology secondary to coronary artery Disease	—
	Non-ischemic cardiomyopathy	—
	Annular dilation	Atrial fibrillation, restrictive cardiomyopathy

MR = mitral regurgitation.
Source: Zoghbi et al. (2017)[13]

Doppler echocardiography (transthoracic echocardiography [TTE]) is the primary imaging used to determine the severity for MR. However, no single Doppler and echocardiographic parameter is sufficiently precise for MR to be quantified in an individual patient (Zoghbi et al., 2017). An integrated approach to determining the severity of MR is suggested by the American Society of Echocardiography (ASE).

Table 2. Grading of the severity of chronic MR by echocardiography (ASE)

	MR Severity*			
	Mild	**Moderate**	**Severe**	
Mitral valve morphology	**None or mild leaflet abnormality** (e.g., mild thickening, calcifications or prolapse, mild tenting)	Moderate leaflet abnormality or moderate tenting	**Severe valve lesions** (DMR: flail leaflet, ruptured papillary muscle, large perforation; FMR: severe tenting, poor leaflet coaptation)	
Left ventricle and left atrium size[a]	Usually normal	Normal or mild dilated	Dilated[b]	
Qualitative Doppler				
Color flow jet area[c]	**Small, central, narrow, often brief**	Variable	Large central jet (> 50% of left atrium) or eccentric wall-impinging jet of variable size	
Flow convergence[d]	**Not visible, transient, or small**	Intermediate in size and duration	**Large throughout systole**	
CWD jet	Faint, partial, parabolic	Dense but partial or parabolic	Holosystolic, dense, triangular	
Semiquantitative				
Vena contracta width (cm)	< 0.3	Intermediate	≥ 0.7 (0.8 for biplane)[e]	
Pulmonary vein flow[f]	**Systolic dominance** (may be blunted in left ventricular dysfunction or atrial fibrillation)	Normal or systolic blunting[f]	Minimal to no systolic flow / **systolic flow reversal**	
Mitral inflow[g]	**A-wave dominant**	Variable	E-wave dominant (> 1.2 m/sec)	
Quantitative[h,i]				
	Mild	**Moderate**	**Moderate to Severe**	**Severe**
EROA, 2D PISA (cm^2)	< 0.2	0.20-0.29	0.30-0.39	≥ 0.40 (may be lower in FMR with elliptical ROA)
Regurgitant volume (mL/beat)	< 0.30	30-44	45-59[h]	≥ 60 (may be lower in low flow conditions)
Regurgitant fraction (%)	< 30	30-39	40-49	≥ 50

ASE = American Society of Echocardiography; CWD = continuous wave Doppler; DMR = degenerative mitral regurgitation; EROA = effective regurgitant orifice area; FMR = functional mitral regurgitation; MR = mitral regurgitation; PISA = proximal isovelocity surface area; ROA = regurgitant orifice area.

Bolded qualitative and semiquantitative signs are considered specific for their MR grade.

*** All parameters have limitations, and an integrated approach must be used that weighs the strength of each echocardiographic measurement. All signs and measures should be interpreted in an individualized manner that accounts for body size, sex, and all other patient characteristics.**

[a] This pertains mostly to DMR.

[b] Left ventricle and left atrium can be within the "normal" range for patients with acute severe MR or with chronic severe MR who have small body size, particularly women, or with small left ventricle size preceding the occurrence of MR.

[c] With Nyquist limit 50-70 cm/sec.

[d] Small flow convergence is usually < 0.3 cm, and large is $1 cm at Nyquist limit of 30-40 cm/sec.

[e] For average between apical two- and four-chamber views.

[f] Influenced by many other factors (left ventricular diastolic function, atrial fibrillation, left atrium pressure).

[g] Most valid in patients > 50 years old and is influenced by other causes of elevated left atrium pressure.

[h] Discrepancies among EROA, regurgitant fraction, and regurgitant volume may arise in the setting of low-flow or high-flow states.

[i] Quantitative parameters can help subclassify the moderate regurgitation group.

Source: Zoghbi et al. (2017)[13]

As shown in Table 3, there is substantial overlap between the ESC/EACTS and AHA/ACC guidelines regarding recommendations for intervention in patients with primary MR.

Table 3. Overview of Recommendations for Intervention in Patients with Primary MR, by Guideline

Recommendations	ESC/ EACTS	AHA/ ACC
Mitral valve repair should be the preferred technique (rather than mitral valve replacement) in patients with severe MR when the results are expected to be durable.	Yes	Yes
Surgery is indicated in symptomatic patients with severe MR and LVEF > 30%.	Yes	Yes
Surgery is indicated in asymptomatic patients with severe MR and LV dysfunction who meet certain criteria.	Yes[a]	Yes[b]
Surgery should be considered in asymptomatic patients with severe MR and preserved LVEF (> 60%) who meet specific LVESD criteria when a durable repair is likely and the repair is performed in a heart valve center.	Yes[c]	Yes[d]
Surgery should be considered in asymptomatic patients with severe MR and preserved LV function (LVEF > 60% and specified LVESD criteria) and atrial fibrillation or pulmonary hypertension (systolic pulmonary pressure > 50 mm Hg).	Yes[e]	Yes[f]
Percutaneous edge-to-edge procedure may be considered in patients with symptomatic severe primary MR who fulfill the echocardiographic criteria of eligibility and are judged inoperable or at high surgical risk by the heart team, avoiding futility.	Yes	—
Transcatheter mitral valve repair may be considered for severely symptomatic patients (NYHA class III/IV) with chronic severe primary MR (stage D) who have favorable anatomy for the repair procedure and a reasonable life expectancy but who have a prohibitive surgical risk because of severe comorbidities and remain severely symptomatic despite optimal GDMT for heart failure.	—	Yes
Mitral valve repair should be considered in symptomatic patients with severe MR and severe LV dysfunction (LVEF < 30% and/or LVESD > 55 mm) refractory to medical therapy when the likelihood of successful repair is high and comorbidity is low.	Yes	—
Mitral valve replacement may be considered in symptomatic patients with severe MR and severe LV dysfunction (LVEF < 30% and/or LVESD > 55 mm) refractory to medical therapy when the likelihood of successful repair is low and comorbidity is low.	Yes	—
Concomitant mitral valve repair or mitral valve replacement is indicated in patients with chronic severe primary MR undergoing cardiac surgery for other indications.	—	Yes
Mitral valve surgery may be considered in symptomatic patients with chronic severe primary MR and LVEF ≤ 30% (stage D).	—	Yes
Concomitant mitral valve repair is reasonable in patients with chronic moderate primary MR (stage B) when undergoing cardiac surgery for other indications.	—	Yes

AHA/ACC = American Heart Association/American College of Cardiology; ESC/EACTS = European Society of Cardiology/European Association for Cardio-Thoracic Surgery; GDMT = guideline-directed management and therapy; LV = left ventricular; LVEF = left ventricular ejection fraction; LVESD = left ventricular end-systolic dimension; MR = mitral regurgitation; NYHA = New York Heart Association.

Note: Stage A: at risk of MR; stage B: progressive MR; stage C: asymptomatic severe MR; stage D: symptomatic severe MR.[6]

[a] LVEF ≤ 60% and/or LVESD ≥ 45 mm.

[b] LVEF 30%-60% and/or LVESD ≥ 40 mm, stage C2.

[c] LVESD 40-44 mm when surgical risk is low and flail leaflet and/or significant left atrial dilatation in sinus rhythm are present.

[d] LVESD < 40 mm; new-onset atrial fibrillation; stage C1; mitral valve repair (rather than mitral valve replacement) specified.

[e] LVESD < 45 mm.

[f] LVESD < 40 mm; new-onset atrial fibrillation; stage C1; high likelihood of a successful and durable repair; mitral valve repair (rather than mitral valve replacement) specified.

Sources: Baumgartner et al. (2017)[73]; Nishimura et al. (2014)[6]; Nishimura et al. (2017)[27]

A search of the literature identified no Australian specific clinical management pathways for patients with mitral regurgitation. The ESC/EACTS (2017) and the AHA/ACC (2017) guidelines were summarised regarding indications for surgical intervention.

The ESC/EACTS guidelines and AHA/ACC guidelines are fairly consistent in their recommendations regarding medical therapy for patients with primary MR (Table 4). The ESC/EACTS guidelines note that medical therapy should be considered for patients with chronic primary MR after the development of heart failure who are not suitable for surgery or when symptoms persist following surgery. Similarly, the AHA/ACC guidelines note that medical therapy for systolic dysfunction is reasonable in symptomatic patients with chronic primary MR and LVEF < 60% in whom surgery is not being considered (class IIa; level of evidence [LOE] B). The ESC/EACTS guidelines and AHA/ACC guidelines also both recommend against the use of vasodilators in certain patients with primary MR.

In the ASE guidelines, severe FMR is defined as EROA ≥ 0.40 cm2 and regurgitant volume ≥ 60 mL/beat. However, the ESC/EACT guidelines specify significantly lower cut-offs (EROA ≥ 0.20 cm2 and regurgitant volume ≥ 30 mL/beat). For classification of severe DMR, the ACC/AHA (2017) and ES/EACT (2017) guidelines are consistent regarding EROA and regurgitant volume (> 0.40 cm2 and ≥ 60 mL/beat). ESC/EACT (2019) guidelines provide different cut-offs for DMR and FMR, but the ASE guidelines do not differentiate between etiology in the classification of severity of MR.

Table 4. Comparison of ESC/EACTS and AHA/ACC Recommended Medical Therapy in Patients with Primary MR

ESC/EACTS	AHA/ACC
ACE inhibitor	ACE inhibitor or ARB
Beta blocker	Beta blocker
Aldosterone antagonist	Aldosterone antagonist (possibly)

ACE = angiotensin-converting enzyme; AHA/ACC = American Heart Association/American College of Cardiology; ARB = angiotensin-receptor blocker; ESC/EACTS = European Society of Cardiology/European Association for Cardio-Thoracic Surgery; MR = mitral regurgitation.

Sources: Baumgartner et al. (2017)[73]; Nishimura et al. (2014)[6]

Provide a rationale for the specifics of the eligible population:

The proposed population for DMR is consistent with that in MBS item 38461 and with the population from the pivotal CLASP IID study.

Are there any prerequisite tests?

Yes

Are the prerequisite tests MBS funded?

Yes

Please provide details to fund the prerequisite tests:

Intervention

Name of the proposed health technology:

Transcatheter mitral valve repair

Describe the key components and clinical steps involved in delivering the proposed health technology:

Patients are screened and assessed for anatomical feasibility for device implantation by transthoracic echocardiography (TTE) and TEE. The TTEs are performed according to specific core laboratory protocols and previously published guidelines defined by the American Society of Echocardiography (ASE) for assessment of valve, ventricular function, and core laboratory measurements (Baumgartner et al., 2017) (Zoghbi et al., 2017). The MR severity is assessed using two-dimensional Doppler echocardiography and graded using the MR severity scale recommended by ASE (Zoghbi et al., 2017). The grading includes none/trace (0), mild (1+), mild-moderate (2+), moderate-severe (3+), and severe regurgitation (4+). Additionally, three-dimensional (3D) images allowing reconstruction of the mitral valve area at baseline and after device implantation are acquired. For assessment of the valve area, multiplanar reconstruction is performed as previously described (Biaggi et al., 2013) (ALtiok et al., 2012). All procedures are guided by TEE.

The Edwards PASCAL Transcatheter Valve Repair system is designed to enable transcatheter valve repair by using clasps and paddles to place a spacer between the native valve leaflets. The clasps can be independently adjusted, if desired, to optimise leaflet capture and fine-tune leaflet position. The paddles are designed to minimise stress concentration on the native leaflets, and the spacer is designed to fill the regurgitant orifice area to reduce MR (Lim et al., 2019).
The PASCAL system includes distinctive features including a central spacer, broader paddles made of pliable nitinol and the possibility of independent leaflet grasping, which may provide technical advantages over MitraClip (Gerçek et al., 2021; Praz et al., 2017).

The procedure is performed under general anaesthesia with hemodynamic monitoring in an operating room or in a hybrid operating room with fluoroscopic and echocardiographic (2D and 3D) imaging capabilities, on the beating heart via a femoral venous approach. The transvenous procedure begins by accessing the femoral vein using conventional percutaneous puncture methods. A guidewire is inserted in the left atrium via transseptal access, and the guide sheath with introducer is inserted over the guidewire across the septum. The implant system is inserted into the guide sheath using a loader and advanced until the flex section exits the guide sheath. The steerable catheter is maneuvered until the implant is centred in the target leaflet zone and appropriately aligned with the mitral annular plane using transesophageal echocardiography (TEE) guidance. The implant position is confirmed and adjusted as necessary to achieve the desired outcome, and then released.

The treatment is carried out by a multidisciplinary heart team including an interventional cardiologist, an echocardiograph, and an anaesthesiologist. The implantation can be done either by the cardiologist or the cardiac surgeon.

Identify how the proposed technology achieves the intended patient outcomes:

Poor leaflet coaptation in MR results in blood leaking backwards through the mitral valve when the heart contracts, reducing the amount of blood that is pumped out to the body (American Heart Association, 2020). In mild MR, the amount of blood that leaks backwards through the valve is minor and has no significant consequences. However, in moderate to severe MR, the left ventricle must work harder to meet the body's demands for oxygenated blood, placing substantial pressure on the heart muscle (American Heart Association, 2020). Over time, this can cause heart failure and leads to reduced survival for patients with MR (Trichon et al., 2003). Left untreated, MR is associated with increased rates of hospitalisation, reduced survival and significant healthcare system costs (Messika-Zeitoun et al., 2020).

By repairing the mitral valve, TMVr results in reduced strain on the heart leading to improved health benefits and survival outcomes.

Does the proposed health technology include a registered trademark component with characteristics that distinguishes it from other similar health components? (

No

Explain whether it is essential to have this trademark component or whether there would be other components that would be suitable:

This application is seeking an amendment to the MBS item 38461, to be device agnostic for all TMVr. Therefore it is not essential to list trademarks in the listing.

Are there any proposed limitations on the provision of the proposed health technology delivered to the patient (For example: accessibility, dosage, quantity, duration or frequency):

Yes

Provide details and explain:

The proposed health technology is to be delivered no more than once every 5 years, in line with the existing MBS item 38461.

If applicable, advise which health professionals will be needed to provide the proposed health technology:

The treatment is carried out by a multidisciplinary heart team including an interventional cardiologist, an imaging cardiologist who is trained on TOE imaging, and an anaesthesiologist. The implantation can be done either by the cardiologist or the cardiac surgeon.

If applicable, advise whether delivery of the proposed health technology can be delegated to another health professional:

N/A

If applicable, advise if there are any limitations on which health professionals might provide a referral for the proposed health technology:

In addition to their professional practice as an interventional cardiologist and imaging cardiologist, they need to receive Edwards product training. The training includes didactic of product and procedure, using the dry model to practice, and physiological model to simulate. Edwards also provides support on screening and onsite support on the case day. Edwards reviews the case and provides feedback, additional training if applicable.

Eligibility for TMVr is determined by the MDHT following a TMVr suitability case conference.

Is there specific training or qualifications required to provide or deliver the proposed service, and/or any accreditation requirements to support delivery of the health technology?

Yes

Provide details and explain:

Physicians and relevant hospital staff (scrub nurse, radiographers, echo technicians) must be accredited by qualified Edwards personnel before involvement in a PASCAL TMVr procedure. Physician accreditation includes an initial intensive training program which includes Procedure Didactic, Echo Didactic, Septal Puncture/Echo recommendations, Dry Bench and simulator training, and device delivery through a Beating Heart Model.

- Device procedure classroom training >1 hour
- Demo device hands-on training > 1hour
- Imaging/Echo classroom training > 1hour
- Case discussion > 1hour

In order to be eligible for the training program the physician must meet the following requirements:

- Be either a cardiologist or a cardiac surgeon.
- Have experience in transseptal technique and have an understanding or experience in structural heart disease (patent foramen ovale, atrial septal defect, aortic valve, etc.).
- Have a multidisciplinary team to support the procedure, including:
- A dedicated echocardiologist for patient screening and to be present during the procedure.
- A cardiac surgeon or interventional cardiologist to provide support.
- Identify five suitable patients prior to training.
- Be able to continue to have a reasonable volume of patients so as to maintain minimum skills levels and optimal patient outcomes.

Indicate the proposed setting(s) in which the proposed health technology will be delivered: (select all relevant settings)

☐ Consulting rooms
☐ Day surgery centre

☐ Emergency Department
☒ Inpatient private hospital
☒ Inpatient public hospital
☐ Laboratory
☐ Outpatient clinic
☐ Patient's home
☐ Point of care testing
☐ Residential aged care facility
☐ Other (please specify)

The procedure is performed in the in-hospital setting with patients admitted.

Is the proposed health technology intended to be entirely rendered inside Australia? (\

Yes

Please provide additional details on the proposed health technology to be rendered outside of Australia:

Provide a response if you answered 'No' to the question above

Comparator

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). This includes identifying health care resources that are needed to be delivered at the same time as the comparator service:

The proposed comparator is TMVr using MitraClip, as outlined in MBS item 38461. This has previously been accepted by MSAC in their consideration of Application No 1662.1.

In order to deliver the comparator service, a MDHT meeting is required to assess eligibility for the procedure. The service is delivered in either a hybrid operating room or a catheterisation laboratory, by a multidisciplinary team including echocardiographers, interventional cardiologists or cardiothoracic surgeons, and cardiac anaesthesiologists (Lim, Kar et al. 2019). Procedures are performed with transoesophageal echocardiographic and fluoroscopic guidance under general anaesthesia.

List any existing MBS item numbers that are relevant for the nominated comparators:

38461 (TMVr), 6082 (co-ordination of TMVr case conference), 6084 (attendance at TMVr case conference)

Please provide a rationale for why this is a comparator:

The proposed comparator of TMVr using the MitraClip system aligns with the current clinical management algorithm, as TMVr is currently specified to be conducted with MitraClip. This

comparator has previously been considered appropriate by the MSAC in Application No. 1662 and 1662.1.

Pattern of substitution – Will the proposed health technology wholly replace the proposed comparator, partially replace the proposed comparator, displace the proposed comparator or be used in combination with the proposed comparator? (please select your response)

☐ None – used with the comparator
☐ Displaced – comparator will likely be used following the proposed technology in some patients
☐ Partial – in some cases, the proposed technology will replace the use of the comparator, but not in all cases
☒ Full – subjects who receive the proposed intervention will not receive the comparator

Please outline and explain the extent to which the current comparator is expected to be substituted:

Patients who receive treatment with PASCAL will not receive treatment with MitraClip. We expect **redacted**% of patients who would previously have been treated with MitraClip to be treated with PASCAL.

Outcomes

(Please copy the below questions and complete for each outcome)

List the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be measured in assessing the clinical claim for the proposed medical service/technology (versus the comparator): (please select your response)

☒ Health benefits
☐ Health harms
☐ Resources
☐ Value of knowing

Safety Outcomes: Patient mortality (procedural), clinical adverse events, procedure-specific adverse events (implant embolism, chordal rupture, implant detachment, vascular complication needing reintervention)

Clinical Effectiveness Outcomes: Survival, freedom from MR grade 3+ or 4+, clinical measures of benefit (NYHA functional class, quality of life, LVEF function, rehospitalisation for CHF)

Outcome description – please include information about whether a change in patient management, or prognosis, occurs as a result of the test information:
N/A, the proposed medical service is not a test.

As a result of the proposed item, patients will be able to receive TMVr using any device currently listed on the ARTG and PL for this indication. This will ensure that patients can receive treatment with the most appropriate device for their cardiac anatomy and permit clinicians the flexibility to decide on the best treatment option.

Proposed MBS items

How is the technology/service funded at present? (for example: research funding; State-based funding; self-funded by patients; no funding or payments):

TMVr is currently funded on MBS specifically for the MitraClip system. Currently, patients can receive MBS-funded TMVr using the MitraClip device only.

PASCAL is available in some public hospital settings.

Please provide at least one proposed item with their descriptor and associated costs, for each population/Intervention: (please copy the below questions and complete for each proposed item)

Proposed item details

MBS item number (where used as a template for the proposed item)	38461
Category number	Category 3
Category description	Therapeutic Procedures
Proposed item descriptor	TMVr, by transvenous or transeptal techniques, for permanent coaptation of mitral valve leaflets, including intra-operative diagnostic imaging, if: (a) the patient has each of the following risk factors: (i) moderate to severe, or severe, symptomatic degenerative (primary) mitral valve regurgitation (grade 3+ or 4+); (ii) left ventricular ejection fraction of 20% or more; (iii) symptoms of mild, moderate or severe chronic heart failure (New York Heart Association class II, III or IV); and (b) as a result of a TMVr suitability case conference, the patient has been: (i) assessed as having an unacceptably high risk for surgical mitral valve replacement; and (ii) recommended as being suitable for the service; and (c) the service is performed: (i) by a cardiothoracic surgeon, or an interventional cardiologist, accredited by the TMVr accreditation committee to perform the service; and (ii) via transfemoral venous delivery, unless transfemoral venous delivery is contraindicated or not feasible; and (iii) in a hospital that is accredited by the TMVr accreditation committee as a suitable hospital for the service; and (d) a service to which this item, or item 38463, applies has not been provided to the patient in the previous 5 years
Proposed MBS fee	$1,568.60
Indicate the overall cost per patient of providing the proposed health technology	$1,568.60
Please specify any anticipated out of pocket expenses	N/A

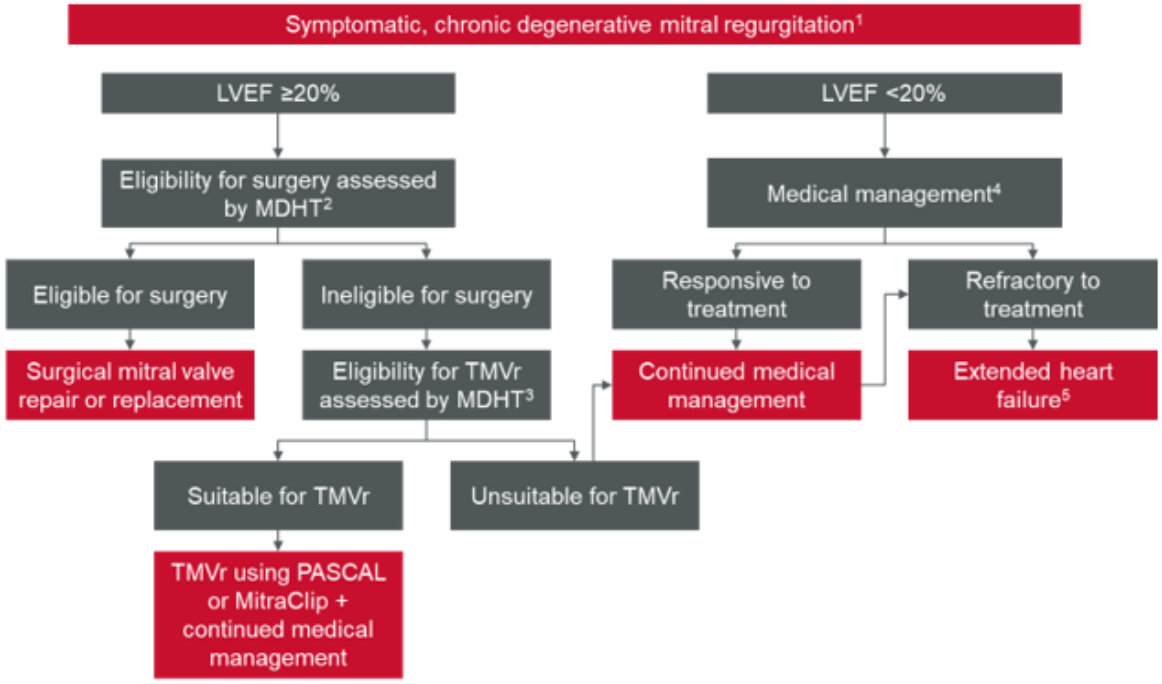
Provide any further details and explain	Provide further details here

Algorithms

Preparation for using the health technology

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, before patients would be eligible for the proposed health technology:

Figure 1-1 Proposed clinical management algorithm for DMR



Notes: 1. Symptomatic DMR defined as NYHA class ≥2 and MR grade 3+ or 4+; 2. Eligibility for surgery determined considering frailty, surgical risk score, major organ system dysfunction, and procedure-specific impediments; 3. Eligibility for TMVr requires MR grade 3+ or 4+, LVEF ≥20%, symptoms of mild, moderate or severe chronic heart failure (NYHA class II, III or IV); 4. Maximally tolerated guideline-directed medical therapy; 5. Extended heart failure treatment included heart transplant, cardiac resynchronisation therapy; ventricular assist devices; and cardiac restraint devices
Abbreviations: LVEF, left ventricular ejection fraction; MDHT, multidisciplinary heart team; TMVr, transcatheter mitral valve repair
Source: Adapted from MSAC Application No. 1192.3 Public Summary Document, Figure 1

The proposed clinical management algorithm for DMR patients is presented in Figure 1-1. This figure is an adaptation of the proposed clinical management algorithm presented in MSAC Application No. 1192.3 (MSAC Application No. 1192.3, Public Summary Document, Figure 1). This clinical management algorithm has previously been considered reasonable by MSAC in their consideration of Application No. 1662.1.

Prior to receiving the proposed health technology, patients will receive testing to determine LVEF, MR severity, and MR aetiology. A MDHT will be held to assess eligibility for TMVr.

Is there any expectation that the clinical management algorithm *before* the health technology is used will change due to the introduction of the proposed health technology?

No

Describe and explain any differences in the clinical management algorithm prior to the use of the proposed health technology vs. the comparator health technology:

N/A, clinical management algorithm and resource utilisation will be the same.

Use of the health technology

Explain what other healthcare resources are used in conjunction with delivering the proposed health technology:

Healthcare resources (TMVr):

Proposed resources to identify eligible population: TTE, TOE, anaesthesiology for TOE, electrocardiography, chest x-ray, cardiac catheterisation, cardiology consultation, surgical consultation, anaesthetic consultation, heart team consultation.

Resources to deliver proposed intervention: Edwards PASCAL Transcatheter Valve Repair System procedure (including two operators), surgical assistant, PASCAL implant and implant system, TOE, anaesthesiology, catheterisation/hybrid lab, theatres, intensive care unit, coronary care unit, TTE, cardiology consultation, pharmaceuticals.

Table 9 presents the associated medical services that are needed to perform the TMVr procedure, this includes any clinic or hospital related costs.

Table 9 Medical services included in the PASCAL procedure

Resource	Reference
Pre-procedural heart team assessment	MBS Item 6082 ($55.75)
	MBS Item 6084 ($41.60)
PASCAL MR implantation fee	MBS item 38461 ($1,568.60)
Anaesthesia	MBS Item 21936
Intra-operative transoesophageal echocardiography	MBS Item 55135, 55126, 55129, 55127,55134
Fluoroscopy	MBS Item 61109
Hospital associated costs	AR-DRG F09B ($17,293) Less prosthesis cost component ($1,947)

Post-procedural/Pre-discharge transoesophageal echocardiography	MBS Item 55126, 55129, 55127, 55134

Explain what other healthcare resources are used in conjunction with the comparator health technology:

The healthcare resources for the MitraClip system will be the same as the PASCAL system.

Describe and explain any differences in the healthcare resources used in conjunction with the proposed health technology vs. the comparator health technology:

There are no differences in healthcare resources between both technologies. The only difference is the TMVr system used during the procedure.

Clinical management after the use of health technology

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, *after* the use of the proposed health technology:

Post-procedure/pre-discharge transoesophageal echocardiography will be provided to assess procedural outcome.

Define and summarise the clinical management algorithm, including any required tests or healthcare resources, *after* the use of the comparator health technology:

Post-procedure/pre-discharge transoesophageal echocardiography are provided to assess procedural outcome.

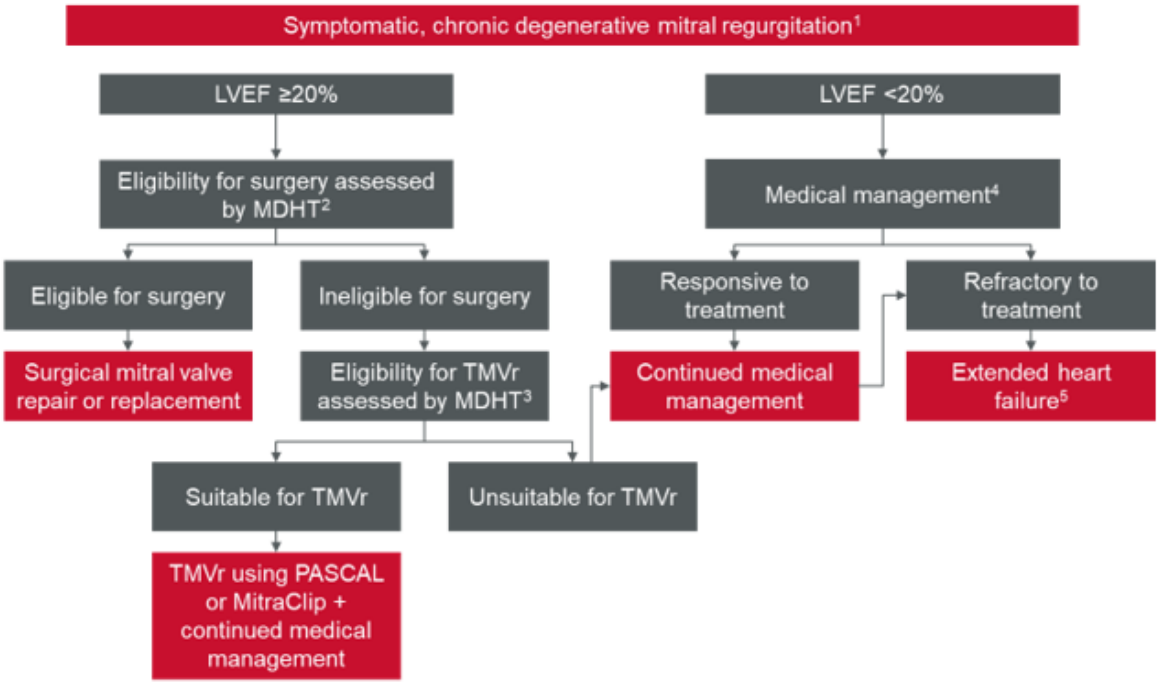
Describe and explain any differences in the healthcare resources used *after* the proposed health technology vs. the comparator health technology:

There are not expected to be any differences in clinical management after the use of the proposed health technology.

Algorithms

Insert diagrams demonstrating the clinical management algorithm with and without the proposed health technology:

Figure 1-1 Proposed clinical management algorithm for DMR



Notes: 1. Symptomatic DMR defined as NYHA class ≥2 and MR grade 3+ or 4+; 2. Eligibility for surgery determined considering frailty, surgical risk score, major organ system dysfunction, and procedure-specific impediments; 3. Eligibility for TMVr requires MR grade 3+ or 4+, LVEF ≥20%, symptoms of mild, moderate or severe chronic heart failure (NYHA class II, III or IV); 4. Maximally tolerated guideline-directed medical therapy; 5. Extended heart failure treatment included heart transplant, cardiac resynchronisation therapy; ventricular assist devices; and cardiac restraint devices
Abbreviations: LVEF, left ventricular ejection fraction; MDHT, multidisciplinary heart team; TMVr, transcatheter mitral valve repair
Source: Adapted from MSAC Application No. 1192.3 Public Summary Document, Figure 1

The proposed clinical management algorithm is shown above. The current clinical management algorithm is not provided, as it is similar to the proposed algorithm with the exception of the TMVr system used.

This algorithm has previously been accepted by MSAC in their consideration of Application No. 1662.1.

Claims

In terms of health outcomes (comparative benefits and harms), is the proposed technology claimed to be superior, non-inferior or inferior to the comparator(s)? (please select your response)

☐ Superior
☒ Non-inferior
☐ Inferior

Please state what the overall claim is, and provide a rationale:

The application will present 12-month data from the randomised CLASP IID trial. This study was a non-inferiority study designed to assess the clinical effectiveness and safety of the PASCAL system compared to MitraClip.

A pre-specified interim analysis of 180 patients from the CLASP IID study has previously shown that PASCAL met the primary and secondary non-inferiority endpoints compared to MitraClip (Lim, Smith et al. 2022). At 30 days, the rate of MAEs was 3.4% in the PASCAL arm vs 4.8% in the MitraClip arm. The absolute difference in 30-day composite MAE rate was -1.5%, with the one-sided 95% CI upper bound of 5.1%. This met the pre-specified non-inferiority margin for this endpoint.

Additionally, the study met its primary effectiveness endpoint of 6-month MR severity. The proportion of patients with MR ≤2+ at 6 months was 96.5% for the PASCAL group and 96.8% for the MitraClip group. The absolute difference was -0.3%, and the upper bound of the one-sided 95% CI was -6.2%, within the pre-specified non-inferiority margin.

The current application will present further data from **redacted** patients from CLASP IID. This data will support the claim of non-inferior safety and effectiveness.

Why would the requestor seek to use the proposed investigative technology rather than the comparator(s)?

The Edwards PASCAL Transcatheter Valve Repair System addresses some of the limitations of other devices, including: a larger implant with wider paddles to potentially reduce the number of implants required for adequate MR reduction; independent clasp control to address complex anatomies and regurgitant jets; a spacer in the centre of the implant to act as a filler in the regurgitant orifice for reduction of MR; working length that allows manoeuvrability even with higher septal puncture heights; and ergonomic controls similar to other Edwards transcatheter product lines which are already familiar to many interventional cardiologists.

Identify how the proposed technology achieves the intended patient outcomes:

Poor leaflet coaptation in MR results in blood leaking backwards through the mitral valve when the heart contracts, reducing the amount of blood that is pumped out to the body (American Heart Association, 2020). In mild MR, the amount of blood that leaks backwards through the valve is minor and has no significant consequences. However, in moderate to severe MR, the left

ventricle must work harder to meet the body's demands for oxygenated blood, placing substantial pressure on the heart muscle (American Heart Association, 2020). Over time, this can cause heart failure and leads to reduced survival for patients with MR (Trichon et al., 2003). Left untreated, MR is associated with increased rates of hospitalisation, reduced survival and significant healthcare system costs (Messika-Zeitoun et al., 2020).

By repairing the mitral valve, TMVr results in reduced strain on the heart leading to improved health benefits and survival outcomes.

DMR patients who have undergone treatment with the PASCAL system continue to demonstrate high survival, low complication rates, significant and sustained improvement in MR accompanied with functional and quality-of-life improvements. These outcomes contribute to the growing body of clinical evidence on the benefits of transcatheter edge-to-edge repair in the treatment of prohibitive risk patients with degenerative mitral regurgitation.

For some people, compared with the comparator(s), does the test information result in:)

A change in clinical management?

A change in health outcome? Yes

Other benefits?

Please provide a rationale, and information on other benefits if relevant:

N/A, the proposed medical service is not a test.

As a result of the proposed item, patients will be able to receive TMVr using any device currently listed on the ARTG and PL for this indication. This will ensure that patients can receive treatment with the most appropriate device for their cardiac anatomy and permit clinicians the flexibility to decide on the best treatment option.

In terms of the immediate costs of the proposed technology (and immediate cost consequences, such as procedural costs, testing costs etc.), is the proposed technology claimed to be more costly, the same cost or less costly than the comparator? (please select your response)

redacted

Provide a brief rationale for the claim:

redacted. The proposed changes to the MBS item will not result in any differences in the fee **redacted**.

Summary of Evidence

Provide one or more recent (published) high quality clinical studies that support use of the proposed health service/technology. At 'Application Form lodgement', please do not attach full text articles; just provide a summary (repeat columns as required).

Identify yet-to-be-published research that may have results available in the near future (that could be relevant to your application). Do not attach full text articles; this is just a summary (repeat columns as required).

	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.	Randomised controlled trial, multicentre	CLASP IID (NCT03706833)	The CLASP IID study is a multicentre RCT designed to assess the safety and effectiveness of PASCAL compared to MitraClip. The study is a non-inferiority study in prohibitive risk DMR 3+/4+ patients. Key endpoints include MAEs, MR severity, NYHA functional class and QoL. **redacted** patients were enrolled and randomly assigned to receive with PASCAL or MitraClip in a 2:1 ratio. Study assessments were performed at baseline, during hospital stay, at discharge, 30 days, 6 months and 1 year, then annually through to 5 years.	1 year outcome: not yet published Pre-specified interim analysis: https://doi.org/10.1016/j.jcin.2022.09.005	1 year outcomes: publication expected in **redacted** Pre-specified interim analysis of 180 patients: December 2022

	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***
2	Prospective, single-arm, observational study Multicentre, international study, 14 sites in 7 countries	CLASP (NCT03170349) Multicentre, prospective, single-arm study of PASCAL Transcatheter Mitral Valve Repair in Patients with Severe Primary and Secondary Mitral Regurgitation (CLASP)	DMR and FMR The study includes both FMR and DMR patients with clinically significant (≥ grade 3+) MR despite OMT, symptomatic NYHA II, III or IV, and who were deemed candidates for TMVr by the local heart team. 109 patients were treated (67% FMR, 33% DMR); mean age 75.5 years, and 57% were NYHA class III or IV. At 1 year, Kaplan-Meier survival was 92% (89% FMR, 96% DMR) with 88% freedom from HF hospitalization (80% FMR, 100% DMR), MR was ≤1+ in 82% of patients (79% FMR, 86% DMR) and ≤2+ in 100% of patients, 88% of patients were NYHA class I or II, and KCCQ score improved by 14 points (p<0.001 for all).	**2-year outcomes:** https://www.sciencedirect.com/science/article/abs/pii/S1936879821006750?via%3Dihub **1-year, 30-day outcomes:** https://www.jacc.org/doi/full/10.1016/j.jcin.2020.06.019 **6-month outcomes:** https://www.tctmd.com/slide/6-month-outcomes-multicenter-prospective-study-novel-pascal-transcatheter-mitral-repair **30-day outcomes:** https://www.jacc.org/doi/full/10.1016/j.jcin.2019.04.034	**30-day outcomes**: n = 62, Lim et al. (2019) n = 109, Webb et al. (2020) n = 117 Szerlip et al. (2021) **6-month outcomes:** n = 62, Lim (2019) **1-year interim outcomes:** n = 62, Webb et al. (2020) n = 85 Szerlip et al. (2021) **2-year outcomes:** n = 36 Szerlip et al. (2021)

Abbreviations: MR, mitral regurgitation; DMR, degenerative mitral regurgitation; FMR, functional mitral regurgitation; TMVr, Transcatheter Mitral Valve repair; HF, heart failure; MC, multicentre; MM, medical management; MN, multinational; NYHA, New York Heart Association; OMT, optimal medical therapy; RCT, randomised controlled trial; SOC, standard of care; RCT, Randomised Controlled Trial; KCCQ, Kansas City Cardiomyopathy Questionnaire; 6MWD, 6 Minute Walk Distance

*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. For yet to be published research, provide high level information including population numbers and whether patients are being recruited or in post-recruitment.

*** If the publication is a follow-up to an initial publication, please advise. For yet to be published research, include the date of when results will be made available (to the best of your knowledge).