Medical Services Advisory Committee (MSAC) Public Summary Document

Application No. 1700– Totally thoracoscopic exclusion of the left atrial appendage for patients with non-valvular atrial fibrillation

Applicant: **AtriCure Inc.**

Date of MSAC consideration: **30-31 March 2023**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, visit the MSAC website

1. Purpose of application

An application requesting Medicare Benefits Schedule (MBS) listing of totally thoracoscopic implantation of an epicardial clip to exclude the left atrial appendage (LAA) for patients with non-valvular atrial fibrillation (NVAF) who have an absolute contraindication to oral anticoagulation (OAC) was received from Atricure Inc. by the Department of Health and Aged Care.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC did not support public funding of totally thoracoscopic exclusion of the left atrial appendage (LAA) for patients with non-valvular atrial fibrillation with absolute contraindications for anticoagulant therapy. MSAC considered that the claims of non-inferior safety and effectiveness of the procedure relative to the comparator (transcatheter occlusion of the LAA) were not strongly supported by the evidence. MSAC considered that this meant that the cost comparison analysis for the economic evaluation was not appropriate (as this would require establishing a clinical claim of non-inferior effectiveness and superior safety). However, MSAC acknowledged that the overall financial cost to the MBS of listing is likely to be low and that it was plausible that there was a low volume clinical need for the procedure among patients with non-valvular atrial fibrillation with absolute contraindications to anticoagulant therapy who were unsuitable for percutaneous LAA closure (LAAC) due to LAA size and morphology, or who have an absolute contraindication to dual anti-platelet therapy which is temporarily required following percutaneous LAA closure until endothelialisation of the device. Therefore, MSAC noted that it was open to considering a resubmission based on better-quality data to support the clinical claims of non-inferior effectiveness and non-inferior/superior safety and/or a narrower population of patients unsuitable for percutaneous LAAC.

Consumer summary
This is an application from AtriCure requesting Medicare Benefits Schedule (MBS) listing of totally thoracoscopic implantation of an epicardial clip (AtriClip) to exclude the left atrial appendage for patients with non-valvular atrial fibrillation who have an absolute contraindication to oral anticoagulation. The left atrial appendage is a small pouch in the top left of the heart that does not play a clear role in the body. In a healthy person, the left atrial appendage causes no issues. However, in

Consumer summary
people with atrial fibrillation (an irregular and often fast heartbeat), blood can pool inside the left atrial appendage. This increases the risk of a blood clot forming, which increases the risk of stroke. This risk is usually managed by taking medications called anticoagulants, which stop blood from clotting quickly. However, some people have certain conditions (like bleeding conditions) that mean they cannot take anticoagulants (contraindicated), as this could make their other conditions worse. For patients who are contraindicated to anticoagulants, an epicardial clip can be surgically placed on the outer surface of the heart at the opening of the left atrial appendage to block it off and stop blood from pooling inside. This application is for an epicardial clip that is placed through a surgical incision (cut) to the chest area, usually beneath the arm (called a thoracoscopic procedure). MSAC considered the evidence for the procedure to be lacking, so was not convinced that it is as safe or effective as other treatments that are currently MBS-reimbursed. MSAC did not consider there to be a strong clinical need for this procedure, as other procedures are available for most of the eligible patients. However, because this treatment would be useful for a small number of patients who cannot receive the other reimbursed treatments, MSAC was open to considering a resubmission if better-quality evidence was available or if the eligible patient group could be properly defined. **MSAC's advice to the Commonwealth Minister for Health and Aged Care** MSAC did not support listing totally thoracoscopic implantation of an epicardial clip to exclude the left atrial appendage. MSAC was not convinced that the procedure is as safe or effective as other treatments. MSAC also considered that the eligible patient population needs to be better defined.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that this application from AtriCure, Inc. is requesting Medicare Benefits Schedule (MBS) listing of totally thoracoscopic implantation of an epicardial clip (AtriClip) to exclude the left atrial appendage (LAA) for patients with non-valvular atrial fibrillation (NVAF) who have an absolute contraindication to oral anticoagulation (OAC).

MSAC noted that it has not previously considered totally thoracoscopic LAA exclusion in patients with NVAF, but it has previously considered percutaneous LAA closure (LAAC) for patients with NVAF who have an absolute contraindication to OAC. At its 67th meeting (July 2016), MSAC supported listing LAAC for stroke prevention in patients with NVAF (MBS item 38276). At its 81st meeting (March–April 2021), MSAC supported an amendment to expand the list of absolute contraindications to OAC therapy.

MSAC noted that the current application is for a new MBS item that would replace, or be an alternative for, current MBS item 38276 (transcatheter occlusion of LAA). MSAC noted that the applicant also has a separate application for LAA exclusion in patients undergoing open cardiac surgery (MSAC Application 1666).

MSAC noted that ESC had questioned the original MBS fee ($1,698.30) because it was substantially higher than the comparator service ($964.45). ESC's main concerns were that the total procedure times were similar and that there was a similar investment in time to undertake extensive training for LAA occlusion. In their pre-ESC response, the applicant revised the proposed fee so that it was the same as the comparator service. However, MSAC noted that, for MBS item 38820 (wedge resection of the lung), the surgical approach for wedge resection, whether that be thoracoscopic or open, does not affect the fee. MSAC considered that the

thoracoscopic AtriClip procedure is more technically demanding than wedge resection, and that it is difficult to compare procedural difficulty between specialties and regarding different procedures – comparing on procedure time alone is simplistic. MSAC considered that, overall, approximate cost equivalence is achieved against percutaneous LAAC with the original MBS fee ($1,698.30). MSAC considered that, generally, MBS reimbursement reflects procedural complexity as opposed to outcome uniformity.

MSAC noted that PASC had suggested that anaesthesia MBS item 20560 could apply to this procedure. MBS item 20560 has a fee of $419.00, which MSAC considered to be too high for the thoracoscopic procedure. The ADAR used MBS item 20528 with a fee of $167.60, which MSAC considered to be too low. MSAC considered that MBS items 20526 (fee of $209.50) and 20540 (fee of $272.35) were more appropriate for the thoracoscopic procedure. MSAC considered that it would be beneficial to approach professional societies about the most appropriate item number for anaesthesia that would apply to the intervention.

MSAC noted from the clinical management algorithm that patients must have an absolute contraindication to lifelong OAC and an increased risk for thromboembolism based on a CHA_2DS_2-VA score of ≥2 to be eligible for this service; this is clearly outlined in the proposed item descriptor. However, MSAC noted that these patients already have access to current MBS item 38276 (transcatheter occlusion of the LAA). MSAC noted that, according to the applicant, 10–20% of patients eligible for percutaneous LAAC because of a lifelong contraindication to OAC are nonetheless unsuitable for this procedure because of LAA size or morphology (although MSAC considered that there were insufficient data to support this claim). MSAC considered that there may also be a small group of patients eligible for Atriclip LAA closure who have contraindications to dual anti-platelet therapy, which is required post-transcatheter LAAC until endothelialisation has been shown on trans-oesophageal echocardiogram. MSAC noted that the pre-MSAC response stated that the patient population for totally thoracoscopic exclusion of the LAA is already very well defined but meant by this that the population had exactly the same definition as the population for the comparator service. However, MSAC considered that the procedure should be restricted to a patient group with an unmet clinical need, namely patients with an ongoing risk of stroke who cannot undergo the percutaneous LAAC procedure (the comparator) and are absolutely contraindicated to OAC.

MSAC noted that the body of evidence for standalone totally thoracoscopic LAA exclusion largely consisted of small, retrospective observational studies with heterogenous eligibility requirements, undefined outcome measures, inadequate follow-up, and risk of selection and reporting bias. MSAC noted that 3 of the 11 identified studies relating to totally thoracoscopic LAA exclusion restricted eligibility to patients with NVAF, of which only one study (45 patients) explicitly mentioned an absolute contraindication to OAC therapy. MSAC noted that data have been pooled for naïve indirect comparison with no consideration of study quality; MSAC acknowledged that, due to the low number of available studies, this may be the only method available. MSAC noted that the pre-MSAC response agreed that this was not ideal, but stated that, in this instance, the non-inferiority analysis would be confounded by the heterogeneity of the groups in favour of the comparison service. However, MSAC considered that the indiscriminate pooling of data was nonetheless unfounded given the poor average quality of the studies included .

Conversely, MSAC noted that the evidence for the comparator included multicentre, randomised controlled trials, with all studies having a low or medium risk of bias. MSAC noted that the

PROTECT-AF (Reddy et al. 2013[1]) and PREVAIL (Holmes et al. 2014[2]) studies were considered in its support of MBS item 38276.

Regarding comparative safety, MSAC noted that the ADAR presented weighted means for the single-arm studies with non-inferiority testing using a margin of 5%, the choice of which was not justified. MSAC considered the comparative findings to be highly uncertain given the heterogeneity across the studies in terms of patient characteristics and study design.

MSAC noted that the AtriClip studies showed a larger range in rates of all perioperative adverse events (0–26%) compared with the comparator studies (2.2–2.8%), which is conceivable given that the totally thoracoscopic surgical approach is more invasive than the percutaneous approach. However, MSAC noted that the definition of a perioperative adverse event varied between the studies. MSAC noted that pericarditis rates of 6.7% and 10.7% were reported in the two AtriClip studies reporting this outcome, while pericarditis was not reported on in any of the comparator studies. Pericardial effusion was reported in all three comparator studies and demonstrated a numerically higher rate (range of 1.9–5.2%) compared with the one AtriClip study that specifically reported this outcome (1.8%).

Similar to the safety data, MSAC considered the reporting of effectiveness data to be generally poor due to the large majority of the studies being small, low-level, observational studies with insufficient follow-up.

MSAC noted that procedural success ranged from 99.4–100% across the AtriClip studies and appeared to be higher than that of the comparator studies (range of 94.7–95.1%), although the definition of procedural success was not defined in the ADAR. However, MSAC considered it likely that complete LAA occlusion would have a higher rate of procedural success, noting that the definition of procedural success for the comparator is <4 mm leak (shown to have no significant difference in major adverse cardiovascular events compared with no leak[3]). Totally thoracoscopic LAA exclusion did not appear to have poorer outcomes than percutaneous LAAC in terms of stroke prevention, but the number of stroke events was low across all studies. Long-term data were also lacking.

Overall, MSAC considered the clinical claim of non-inferior safety and effectiveness was not confirmed. There was a lack of direct comparative evidence for the proposed service and comparator, and poor-quality evidence for the proposed service, which largely comprised of single-arm, observational studies with inadequate follow-up and a high risk of selection and reporting bias.

MSAC noted that the economic evaluation was based on a cost-comparison analysis. However, MSAC noted that, according to the 2021 MSAC Guidelines (p. 203), a cost analysis is only considered acceptable in cases where "the proposed health technology is demonstrated to be no worse in terms of effectiveness but has a superior safety profile compared with the comparator". MSAC considered that if the procedure was restricted to a defined population who are unable to have percutaneous LAAC, then a cost-utility analysis may be more appropriate.

MSAC noted that the ADAR reported the cost per year to be $21,733 ($21,841 per successful exclusion of LAA) for the intervention and $22,597 ($23,811 per successful exclusion of LAA) for

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[1] Reddy VY et al. (2013). Percutaneous left atrial appendage closure for stroke prophylaxis in patients with atrial fibrillation: 2.3-year follow-up of the PROTECT AF (Watchman Left Atrial Appendage System for Embolic Protection in Patients with Atrial Fibrillation) Trial. *Circulation* 127(6):720-729.

[2] Holmes Jr DR et al. (2014). Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial. *J Am Coll Cardiol* 64(1):1-12.

[3] Nguyen A et al. (2019). Peridevice leak after left atrial appendage closure: incidence, risk factors, and clinical impact. *Can J Cardiol* 35(4):405-412.

the comparator. The commentary recalculated these values to be $21,272 for the intervention and $20,551 for the comparator. However, MSAC noted that neither the ADAR nor commentary used the lower item number price agreed to in the pre-ESC response (approximately $730 less). MSAC noted that the key driver of the cost were prostheses costs (particularly for the comparator) and hospital costs (particularly for the intervention). No sensitivity analyses were conducted.

MSAC noted that the captured risk of stroke at 1 year was based on data from single-arm studies that were underpowered for this outcome, with very few events reported. Additionally, the cost comparison did not take periprocedural complications into consideration, nor did it adequately consider downstream costs. Robust clinical data to support these inputs were also lacking.

MSAC noted that the cost of the AtriClip PRO2 LAA Exclusion System is substantially higher than the Protheses List benefit for the AtriClip FLEX LAA Exclusion System, which is indicated for open occlusion of the LAA.

MSAC noted that a market-share approach was used to inform utilisation estimates for the financial impact analysis. The estimated usage was 40 patients in year 1, increasing to 242 patients in year 6. MSAC considered that uptake of the proposed service will likely be restricted due to a limitation in the number of cardiothoracic surgeons and centres than can perform this procedure. Additionally, the use of the service outside the proposed patient population is unlikely given that it is the same population currently eligible for percutaneous LAA closure and the patient's absolute contraindication to lifelong OAC must be documented by an independent medical practitioner.

MSAC noted that MBS listing could potentially grow the market because the proposed service would provide an option for 10–20% of patients who, according to the applicant, are eligible for percutaneous LAAC but are unsuitable due to LAA size or morphology. If the market share does increase over time, the estimated budget impact increases significantly, from $45,575 in year 1 to $266,904 in year 6.

MSAC noted that the financial impact analysis did not consider out-of-pocket costs, which may be significant due to the specialised nature of the procedure and the small number of providers available. MSAC noted that the pre-MSAC response stated that it is expected that there would be minimal to no out-of-pocket costs; currently, providers are offering the service without out-of-pocket costs through hospital funding. However, MSAC considered that historical data show that once a service is available, out-of-pocket costs do occur.

MSAC also noted that it is anticipated that there will be a reduction in costs to the Pharmaceutical Benefits Scheme associated with reduced use of anti-coagulation therapy.

MSAC reiterated that it was important that patients understand how to interpret the risk of stroke when considering treatments – that is, that they do not prevent strokes from occurring, but reduce the risk of stroke. MSAC considered that it was important that a heart team is involved to discuss the correct approach with a patient.

Overall, MSAC considered that the claim of non-inferior/superior safety and non-inferior effectiveness is not supported. Given that the claim of non-inferior effectiveness and superior safety is not supported with the provided evidence, a cost-comparison analysis is not appropriate. Furthermore, the unmet clinical need is inadequately explored by the applicant.

Before resubmitting to MSAC, MSAC advised that the applicant would need to provide better-quality data to support the clinical claims, particularly more long-term data. It appears that, currently, no high-quality studies are in progress. If better-quality data are not likely, then a better characterisation of unmet clinical need is necessary (an application with a narrower population, e.g. those unsuitable for LAAC), as well as periprocedural complications and associated costs.

MSAC also advised that the economic evaluation would need to be redone before a resubmission.

4. Background

MSAC has not previously considered totally thoracoscopic LAA exclusion in NVAF patients.

The applicant is currently preparing a separate ADAR for LAA exclusion in patients undergoing open cardiac surgery:

- MSAC application 1666 – Exclusion of the LAA via surgical epicardial clip implantation concomitant to open cardiac surgery for patients with AF

MSAC has previously considered percutaneous LAA closure (LAAC) for patients with NVAF:

- MSAC 62nd Meeting November 2014 – MSAC application 1347 – Transcatheter occlusion of the LAA for patients with NVAF
- MSAC 67th Meeting July 2016 – MSAC application 1347.1 – LAA closure for stroke prevention in patients with NVAF
- MSAC 81st Meeting March/April 2021 – MSAC application 1615 – Transcatheter occlusion of the LAA for patients with NVAF

MSAC supported listing of percutaneous LAAC in July 2016 (MBS item 38276) and supported amendment to expand the list of absolute contraindications to oral anticoagulation therapy (OAT) in March/April 2021.

The PICO Confirmation for MSAC application 1700 was considered by the PICO Confirmation Advisory Sub-Committee (PASC) at their meeting in April 2022. 'For further information see the PICO Confirmation.

5. Prerequisites to implementation of any funding advice

The implantable medical device is a single-use, class III device (AtriClip PRO2 LAA Exclusion System) that is currently included in the ARTG for epicardial exclusion of the LAA (ARTG number 308864, start date 31st August 2018). The proposed cost of the device is $6,800.

At the current time, no other sponsors and/or manufacturers have a similar medical device for epicardial use in the Australian marketplace.

For the proposed service to be accessible for patients in the private setting, there is a requirement for the AtriClip PRO2 device to be included on the Prostheses List (PL).

The AtriClip LAA Exclusion System comes in several models that are indicated for use either as standalone minimally invasive surgery or concomitant to open cardiac surgery. The only AtriClip device listed on the PL (AtriClip FLEX) is for open occlusion of the LAA (Billing Code ZZ066, Benefit $1,097).

6. Proposal for public funding

Proposed MBS item descriptor

The Applicant proposed the creation of a new MBS item (and Explanatory Note) for the proposed therapeutic service, based on MBS item 38276 (and Explanatory Note TN.8.132) for percutaneous LAAC, with an almost identical wording to target the same patient population.

Similar to MBS item 38276, the proposed descriptor does not specify the device type or whether the procedure is standalone. PASC advised that around 70% of all totally thoracoscopic LAA exclusion procedures would be standalone (which is consistent with the clinical evidence in Section 2 of the ADAR), but the procedure could also be performed concomitant to radiofrequency ablation (MBS items 38512 and 38515) or mini thoracotomy valve surgery.

The proposed item descriptor precludes co-claiming with cardiac catheterisation items. This is appropriate for the percutaneous LAAC procedure where fluoroscopy is used to guide device placement, but it is not relevant for totally thoracoscopic LAA exclusion. The proposed and comparator procedures both require imaging with transoesophageal echocardiography (TOE). The applicant's pre-ESC response accepted that that the precluding of co-claiming for cardiac catheterisation items should be removed and proposed instead that co-claiming with the following items should be precluded – 38485, 38499, 38516 and 38517.

The Ratified PICO Confirmation notes that the service is delivered once per lifetime of a patient; however, this is not specified in the proposed MBS item or Explanatory Note. The ADAR does not discuss or provide clinical evidence relating to device removal or re-implantation.

Table 1 Proposed new MBS item for totally thoracoscopic LAA exclusion in patients with NVAF

Category 3 – THERAPEUTIC PROCEDURES GroupT8 – Surgical Operations
MBS item XXXXX Totally thoracoscopic exclusion of the left atrial appendage for **stroke prevention in** patients with non-valvular atrial fibrillation, if: (a) the patient is at increased risk of thromboembolism demonstrated by: (i) a prior stroke (whether of an ischaemic or unknown type), transient ischaemic attack or non-central nervous system systemic embolism; or (ii) at least 2 of the following risk factors: (A) an age of 65 years or more; (B) hypertension; (C) diabetes mellitus; (D) heart failure or left ventricular ejection fraction of 35% or less (or both); (E) vascular disease (prior myocardial infarction, peripheral artery disease or aortic plaque); and (b) the patient has an absolute and permanent contraindication to oral anticoagulation (confirmed by written documentation that is provided by a medical practitioner, independent of the practitioner rendering the service); a~~(c) the service is not associated with a service to which item 38200, 38203, 38206 or 38254 applies (H)~~ Multiple Operation Rule (Anaes.) (Assist.) (See para TN.8.YYY of explanatory notes to this Category)
Fee: $1698.30 Benefit: 75% = $1273.73
Explanatory note TN.8.YYY Totally thoracoscopic exclusion of the left atrial appendage for stroke prevention (item XXXXX) **Eligibility requirements for Item XXXXX** This item is intended for use in patients where an independent medical practitioner has documented an absolute and permanent contraindication to oral coagulation. The medical practitioner who has documented this contraindication should not have been involved in any decision to provide the service or the actual provision of the service, and is not engaged in the same or a similar group of practitioners. The following list provides examples of the conditions for which this item is intended:

Category 3 – THERAPEUTIC PROCEDURES GroupT8 – Surgical Operations
i. A previous major bleeding complication experienced whilst undergoing treatment with oral anticoagulation therapy without remedial cause, or ii. History of intracranial, intraocular, spinal, retroperitoneal or atraumatic intra-articular bleeding, or iii. Chronic, irreversible, recurrent gastrointestinal bleeding of any cause (eg, radiation proctitis, gut angiodysplasia, hereditary haemorrhagic telangiectasia, gastric antral vascular ectasia (GAVE), portal hypertensive gastropathy, refractory radiation proctitis, obscure source), or iv. Life-long spontaneous impairment of haemostasis, or v. A vascular abnormality predisposing to potentially life-threatening haemorrhage, or vi. Irreversible hepatic disease with coagulopathy and increased bleeding risk (Child Pugh B and C), or vii. Receiving concomitant medications with strong inhibitors of both CYP3A4 and P-glycoprotein (P-gp), or viii. Severe renal impairment defined as creatinine clearance (CrCL) < 15 ml/min or undergoing dialysis and where warfarin is inappropriate, or ix. Known hypersensitivity to the direct oral anticoagulant (DOAC) or to any of the excipients. This item is not intended for use in patients with a relative contraindication to oral anticoagulation. The procedure is performed as a hospital service **by cardiothoracic surgeons with training in video-assisted thoracoscopic surgery**.

Source: ADAR, Section 1, Table 5
Note: Assessment Group suggested amendments are shown in **blue text**.

The proposed service is intended to be performed in-hospital by cardiothoracic surgeons with total thoracoscopy skills in a procedure room with video-assisted thoracoscopic display capabilities. The applicant estimated that there are currently five centres and seven operators, inclusive of public and private, in Australia performing the proposed service. The procedure is performed under general anaesthesia and requires a hospital stay of one or two nights.

Proposed schedule fee

The proposed fee ($1,698.30) is higher than the fee for percutaneous LAAC ($964.45) and was derived by the Applicant in consultation with the Australian and New Zealand Society of Cardiac and Thoracic Surgeons (ANZCTS). The totally thoracoscopic implantation procedure normally takes 20-40 minutes to complete but the total procedure time is around 60 minutes (similar to percutaneous LAAC). The higher fee is intended to reflect the specific skills and investment in time in thoracoscopic training. However the applicant's pre-ESC response acknowledged the feedback that the proposed fee was significantly higher than for percutaneous LAAC and was willing to revise the proposed fee to match that of the comparator i.e. $964.45.

Training requirements are not defined in the proposed MBS item (or Explanatory Note) but could be incorporated as 'cardiothoracic surgeons with training in video-assisted thoracoscopic surgery' (added as blue text to the proposed Explanatory Note above). The applicant's pre-ESC response accepted the suggested amendment to the item descriptor such that the service must be provided by cardiothoracic surgeons with training in video-assisted thoracoscopic surgery.

MSAC supported retaining the original proposed schedule fee – please see above in section 3.

7. Population

The patient population specified in the Ratified PICO Confirmation and in the ADAR are patients with NVAF who have an absolute contraindication to life-long OAC therapy and are at risk of

stroke based on a CHA_2DS_2-VASc score of ≥2. Patients with no or a relative contraindication to OAT are not eligible to receive the proposed service or percutaneous LAAC.

As the patient population for the proposed service is identical to that of the percutaneous LAAC procedure, it is expected that totally thoracoscopic LAA exclusion will be used as an alternative therapeutic solution for this specific patient population. The Applicant expects that the proposed service will take no more than around 30% market share due to (i) the limited number of cardiothoracic surgeons with total thoracoscopy skills relative to the number cardiologists with interventional skills (interventional cardiologists and electrophysiologists), (ii) the limited number of sites with cardiothoracic surgery services compared to number of sites with interventional cardiology services, and (iii) referral pathways currently do not involve consultation with cardiothoracic surgeons. Furthermore, there are conditions that preclude totally thoracoscopic implantation of the epicardial clip, such as pericardial adhesions as a result of previous cardiothoracic surgery, and the presence of LAA thrombus.

For some patients, totally thoracoscopic LAA exclusion may provide a more attractive therapeutic solution because, unlike percutaneous LAAC, post-procedure antiplatelet therapy is generally not required because the device is placed on the epicardial surface. Totally thoracoscopic LAA exclusion may also be the only treatment option for a small number of patients who have an absolute contraindication to OAC and who are unsuitable for percutaneous LAAC due to LAA size and morphology.

Leakage outside the target population is unlikely because it is the same population currently eligible for percutaneous LAAC and the patient's absolute contraindication to life-long oral anticoagulation must be documented by an independent medical practitioner.

8. Comparator

The comparator in the Ratified PICO Confirmation and the ADAR is percutaneous LAAC. The percutaneous LAAC procedure duration is comparable to the proposed procedure, taking 30-60 minutes with general or local anaesthesia. The procedure is performed by either an interventional cardiologist or cardiac electrophysiologist who implants the percutaneous device through femoral venous access under guidance of fluoroscopy and TOE. The procedure is performed either as a day procedure or with a single overnight stay. The standard of care after percutaneous LAAC is dual antiplatelet therapy (DAPT) for 4-12 weeks and a single-agent antiplatelet therapy (APT) thereafter.

As mentioned in Section 2 of this Executive Summary, MSAC supported listing of percutaneous LAAC in July 2016 (with the subsequent introduction of MBS item 38276) and supported amendment to expand the list of absolute contraindications to OAT in March/April 2021. Table 2 provides the current item descriptor and fee. The item includes cardiac catheterisation and fluoroscopy guidance.

Table 2 MBS item 38276 for percutaneous LAA closure

Category 3 – THERAPEUTIC PROCEDURES GroupT8 - Surgical Operations
MBS item 38276 Transcatheter occlusion of left atrial appendage, and cardiac catheterisation performed by the same practitioner, for stroke prevention in a patient who has non-valvular atrial fibrillation, if: (a) the patient is at increased risk of thromboembolism demonstrated by: (i) a prior stroke (whether of an ischaemic or unknown type), transient ischaemic attack or non-central nervous system systemic embolism; or

(ii) at least 2 of the following risk factors:

(A) an age of 65 years or more;
(B) hypertension;
(C) diabetes mellitus;
(D) heart failure or left ventricular ejection fraction of 35% or less (or both);
(E) vascular disease (prior myocardial infarction, peripheral artery disease or aortic plaque); and

(b) the patient has an absolute and permanent contraindication to oral anticoagulation (confirmed by written documentation that is provided by a medical practitioner, independent of the practitioner rendering the service); and

(c) the service is not associated with a service to which item 38200, 38203, 38206 or 38254 applies

(H)

Multiple Operation Rule

(Anaes.) (Assist.)

Fee: $964.45 Benefit: 75% = $723.35

TN.8.132 Transcatheter occlusion of left atrial appendage for stroke prevention (item 38276)

Eligibility requirements for Item 38276

This item is intended for use in patients where an independent medical practitioner has documented an absolute and permanent contraindication to oral coagulation. The medical practitioner who has documented this contraindication should not have been involved in any decision to provide the service or the actual provision of the service, and is not engaged in the same or a similar group of practitioners.

The following list provides examples of the conditions for which this item is intended:

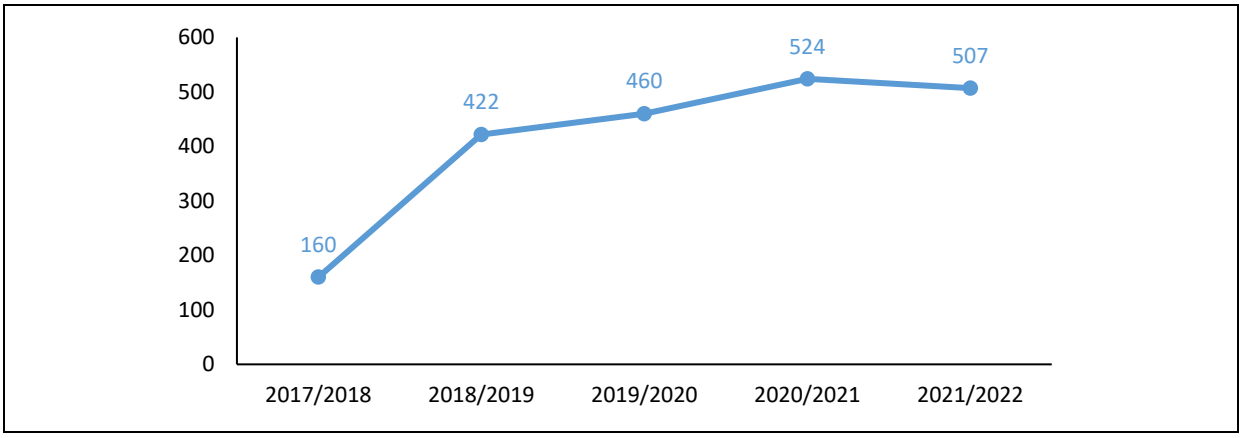
(i) A previous major bleeding complication experienced whilst undergoing treatment with oral anticoagulation therapy without remedial cause, or
(ii) History of intracranial, intraocular, spinal, retroperitoneal or atraumatic intra-articular bleeding, or
(iii) Chronic, irreversible, recurrent gastrointestinal bleeding of any cause (eg, radiation proctitis, gut angiodysplasia, hereditary haemorrhagic telangiectasia, gastric antral vascular ectasia (GAVE), portal hypertensive gastropathy, refractory radiation proctitis, obscure source), or
(iv) Life-long spontaneous impairment of haemostasis, or
(v) A vascular abnormality predisposing to potentially life threatening haemorrhage, or
(vi) Irreversible hepatic disease with coagulopathy and increased bleeding risk (Child Pugh B and C), or
(vii) Receiving concomitant medications with strong inhibitors of both CYP3A4 and P-glycoprotein (P-gp), or
(viii) Severe renal impairment defined as creatinine clearance (CrCL) < 15 ml/min or undergoing dialysis and where warfarin is inappropriate, or
(ix) Known hypersensitivity to the direct oral anticoagulant (DOAC) or to any of the excipients.

This item is not intended for use in patients with a relative contraindication to oral anticoagulation.

Source: MBS Online, accessed 28 November 2022

The number of services for MBS item 38276 appears to have reached a stable number, with little growth over the last three years (see Figure 1). However, the impact of the pandemic on elective surgery needs to be taken into consideration when interpreting these data.

Figure 1 Number of services for MBS item 38276 for the period 2017-18 to 2021-22



Source: Medicare Item Reports, 28 November 2022

Several devices for percutaneous LAAC are listed on the PL: WATCHMAN (Boston Scientific, Billing Code BS332), WATCHMAN FLX (Boston Scientific, Billing Code BS384) and Amplatzer Amulet (Abbott Medical, Billing Code SJ395). The PL benefit for each of the three devices is $11,269.

9. Summary of public consultation input

Consultation input was received from one (1) professional organisation and one (1) consumer organisation:

- the Australian and New Zealand Society for Vascular Surgery (ANZSVS), and
- Hearts4Heart.

The consultation feedback was supportive of public funding for totally thoracoscopic LAA exclusion for patients with non-valvular atrial fibrillation who have an absolute contraindication to life-long oral anticoagulant therapy and are at risk of stroke.

The main benefits of publicly funding the totally thoracoscopic LAA procedure noted in the consultation feedback included:

- improved management of the embolic risk for patients with atrial fibrillation where patients are considered too high risk for standard therapy, resulting in decreased number of patients with embolic complications from atrial fibrillation;
- safe, effective occlusion of the LAA;
- providing an option for patients who are not suited to taking blood thinning medications and is recommended for patients who have had a stroke previously;
- the short duration of the procedure, and no need for the patient to take blood thinning medication post-procedure.

The main disadvantages of the totally thoracoscopic LAA procedure identified in the consultation feedback were the possible complications from intra-thoracic surgery.

10. Characteristics of the evidence base

The Applicant's literature search identified ten published studies and one unpublished study on totally thoracoscopic LAA exclusion, all using the AtriClip device. The search did not identify any direct head-to-head RCTs of AtriClip versus a percutaneous LAA occlusion device, or RCTs that

could be used to support an indirect comparison via a common comparator arm. In the absence of these studies, non-comparative observational studies were included.

Three comparator studies (reported in four publications) were included. Two of the comparator studies, PROTECT-AF and PREVAIL, were provided as key evidence to support MBS listing of percutaneous LAAC. Five-year follow up data are available for PROTECT-AF and PREVAIL; however, the publication reporting this long-term follow-up was not identified in the Applicant's literature search. An additional 27 full texts on percutaneous LAAC were excluded by the Applicant on the basis of inferior quality (criteria were not defined).

The key features of these studies are summarised in Table 3, with studies ordered from largest to smallest study size. One included study on the AtriClip device has been omitted by the Assessment Group because patients with NVAF were specifically excluded from this study. The AtriClip studies are all single arm for the purposes of this assessment and the majority report on the initial experience of a single surgeon or institution. The studies were mostly underpowered for effectiveness outcomes, with study sizes ranging from 4 to 243 patients. Follow-up was limited, ranging from one week post discharge to 2.3 years. In contrast, the studies reporting on the comparator – percutaneous LAAC – were single arm studies, two from well conducted multicentre RCTs, with study sizes ranging from 150 to 463 patients.

Table 3 Key features of the included evidence

References	N	Design/duration	Risk of bias	Patient population	Outcome(s)	Use in economic evaluation
Intervention						
Friedman 2022	243 in AtriClip group	RS; propensity matched to control group 12 mo	*High*	AF with high risk of stroke and bleeding, not on OACs	Safety Periprocedural AE Major bleeding events Post procedural AE Effectiveness Stroke Systemic embolism	-
Cartledge 2022	175	RS; MC; OB 12.5 mo	*High*	NVAF with high risk of stroke or bleeding or with intolerance to OAC	Safety Periprocedural AE Major bleeding events Effectiveness Procedural success CV and all-cause mortality Stroke	-
Wang unpublished	56 stand-alone procedure group	PS; SC; OB 2.3 yr	*Low*	AF with contraindications to anticoagulant therapy	Safety Major bleeding events Effectiveness Procedural success CV and all-cause mortality Failure and reintervention rate Stroke	Stroke
Branzoli 2020	45	PS; SC; OB 16.4 mo	*High*	NVAF with absolute contraindications to (N)OAC's or at high risk of life-threatening bleeding if on APT	Safety Periprocedural AE Major bleeding events Post procedural AE Effectiveness Procedural success Stroke	Stroke

References	N	Design/duration	Risk of bias	Patient population	Outcome(s)	Use in economic evaluation
Antaki 2021	42	RS; SC; OB 12.4 mo	*High*	AF with high-risk of thromboembolic stroke and intolerance to OACs	Safety Periprocedural AE Major bleeding events Effectiveness Procedural success CV and all-cause mortality Stroke	Stroke
Smith 2017	24	RS; SC; OB 1 wk	*High*	AF with high risk for stroke and bleeding such that OAC is contraindicated	Safety Periprocedural AE Major bleeding events Effectiveness Procedural success CV and all-cause mortality Stroke	-
Franciulli 2020	20	RS; SC; OB 6 mo	*High*	NVAF with high thrombotic and bleeding risk and contraindicated to OAC and APT	Safety Periprocedural AE Major bleeding events Post procedural AE Effectiveness Procedural success CV and all-cause mortality	-
Akca 2017	5	CS 7.2 mo	*High*	AF with contraindication to OAC and APT or previous failed percutaneous device implantation	Safety Periprocedural AE Effectiveness Procedural success CV and all-cause mortality Stroke	-
Suwalski 2015	4	CS 2 mo	*High*	AF with OAC intolerance or suboptimal/unstable level	Safety Periprocedural AE Major bleeding events Effectiveness Procedural success CV and all-cause mortality Failure and reintervention rate Stroke	-
Fleerakers 2020	4	CS 4.5 mo	*High*	AF and LAA containing thrombus	Safety Periprocedural AE Post procedural AE Effectiveness Stroke	-
Comparator						
Reddy 2013 (PROTECT-AF)	463	RCT; MC 2.3 yr and 5 yr	*Low*	NVAF at risk of stroke	Safety Periprocedural AE Effectiveness CV and all-cause mortality Systemic embolism Stroke	Stroke
Viles-Gonzalez 2012	445	Post hoc analysis 10.9 mo	*Low*	Patients from the PROTECT AF trial (post hoc analysis)	Safety Major bleeding events Effectiveness Stroke	-

References	N	Design/duration	Risk of bias	Patient population	Outcome(s)	Use in economic evaluation
Holmes 2014 (PREVAIL)	407	RCT; MC 11.8 mo and 5 yr	*Low*	NVAF at risk of stroke	<u>Safety</u> Periprocedural AE Major bleeding events <u>Effectiveness</u> Procedural success CV and all-cause mortality Systemic embolism Stroke	Stroke
Reddy 2013 (ASAP)	150	PS; MC; NR 14.4 mo	*Moderate*	NVAF at risk of stroke with contraindications to OAC	<u>Safety</u> Periprocedural AE Major bleeding events <u>Effectiveness</u> Procedural success CV and all-cause mortality Failure and reintervention rate Stroke	Stroke

Source: Derived from ADAR, Section 2A.2, Commentary Table 7
AE = adverse events; CS = case series; CV = cardiovascular; DB = double blind; MC = multicentre; mo = months; NR = non-randomised; OB = observational; OL = open label; OS = overall survival; PFS = progression-free survival; PS = prospective; R = randomised; RS = retrospective; SC = single centre; YR = years.

There are several notable issues with the included studies, including variable definitions of what constitutes an absolute contraindication to OACs, variable definitions of perioperative outcomes and events reported at unspecified time points. Additionally, the majority of studies included patients who do not strictly meet the population specified in the Ratified PICO. Only six studies (three reporting on AtriClip) specifically included an NVAF population.

All of the AtriClip studies were judged to be at moderate or high risk of bias in the ADAR, with the exception of three studies, one of which is not eligible for inclusion and another that is unpublished. These studies have been reassessed by the Assessment Group to be high risk of bias based on undefined outcome measures, inadequate length of follow-up, and poorly described or non-existent statistical methods.

The ADAR did not include the patient characteristics from each of the studies, limiting the ability to understand the comorbidities of the population and the comparability between the evidence base for the intervention and comparator. Additionally, key outcomes reported in study publications, such as mortality and failure rates, were not reported in the ADAR. However the applicant's pre-ESC response noted that while failure rates were not reported in the Atriclip studies, an inverse rate to procedural success (i.e. 100% minus the procedural success rate) can be used to infer failure rates. This would be a conservative approach, as procedural success is not dictated solely by device failure rates, and thus would likely overestimate the true rate. The pre-ESC response noted procedural success was reported in all the included studies for the intervention except Friedman [4] and that all these studies reported procedural success of 100% except Cartledge[5] (99%) and Yoshimoto[6] (97.5%). The inferred failure rates from these two

[4] Friedman D, et al. (2022) 'Real world outcomes of minimally invasive epicardial surgical left atrial appendage exclusion in atrial fibrillation patients with high risk of stroke and bleeding', *Europace*, 24(Supplement_1), euac053-296.

[5] Cartledge R, et al. (2022). 'Standalone epicardial left atrial appendage exclusion for thromboembolism prevention in atrial fibrillation', *Interactive CardioVascular and Thoracic Surgery*, 34(4), 548-555

[6] Yoshimoto, A., et al. (2021). 'Early and middle-term results and anticoagulation strategy after left atrial appendage exclusion using an epicardial clip device', *Annals of Thoracic and Cardiovascular Surgery,* 27(3), 185

studies were 1% and 2.5% respectively which was lower than the failure rates reported in the comparator studies PREVAIL[7] (4.9%) and ASAP[8] (5.3%).

11. Comparative safety

As the majority of the AtriClip studies were small, retrospective observational studies, the reporting of safety data was generally poor, and the completeness of the data collection was variable. Furthermore, studies that reported the initial experience of the surgeon/institution in using the totally thoracoscopic LAA exclusion technique inevitably incorporated the learning curve. In contrast, two of the comparator studies were RCTs with more rigorous study conduct and pre-specified safety outcomes and analyses.

The ADAR presents weighted means for the single arm studies with non-inferiority testing using a margin of 5%, the choice of which was not justified. The comparative findings are highly uncertain given the heterogeneity across the studies in terms of patient characteristics and study design, the poor reporting of adverse events in many of the AtriClip studies, the low total event rates reported and the generally high risk of bias across the studies.

Pericardial effusion was reported in all three comparator studies and demonstrated a numerically higher rate (range 1.9–5.2%) compared with the one AtriClip study that specifically reported this outcome (1.8%). Pericarditis rates of 6.7% and 10.7% were reported in the two AtriClip studies reporting this outcome; pericarditis was not reported on in any of the comparator studies. Cardiac tamponade and major bleeding events were low across all studies.

Overall, the AtriClip studies showed a larger range in rates of all perioperative adverse events (0–26%) compared with the comparator studies (2.2–2.8%). However, the definition of a perioperative adverse event varied between the studies, and no firm conclusions can be drawn.

Safety conclusions

The evidence for the safety of the proposed service is based entirely on low level, single arm studies and the safety data were insufficient to draw a conclusion of non-inferiority of totally thoracoscopic LAA exclusion compared with percutaneous LAA exclusion, either perioperatively or over the longer term. It is possible that thoracoscopic LAA exclusion may be associated with an increased risk of perioperative adverse events, which is conceivable given that the totally thoracoscopic surgical approach is more invasive than the percutaneous approach.

However the applicant's pre-ESC response contended that it is more likely given the total lack of reported adverse events and extremely low adverse events rate reported in included studies and despite including studies where the institution was subject to device learning curves (as acknowledged by the commentary) that totally thoracoscopic LAA exclusion has a lower perioperative adverse event rate.

[7] Holmes D, et al. (2014). 'Prospective randomized evaluation of the Watchman Left Atrial Appendage Closure device in patients with atrial fibrillation versus long-term warfarin therapy: the PREVAIL trial', *Journal of the American College of Cardiology*, 64(1), 1-12

[8] Reddy V, et al. (2013). 'Left atrial appendage closure with the Watchman device in patients with a contraindication for oral anticoagulation: the ASAP study (ASA Plavix Feasibility Study With Watchman Left Atrial Appendage Closure Technology)', *Journal of the American College of Cardiology*, 61(25), 2551-2556.

12. Comparative effectiveness

Similar to the safety data, the reporting of effectiveness data was generally poor due to the large majority of the studies being small, low level, observational studies with insufficient follow-up.

Procedural success ranged from 99.4–100% across the AtriClip studies and appears to be higher than that of the comparator studies (94.7–95.1%), although the definition of procedural success has not been defined in the ADAR.

The total number of stroke events was low across all studies and long-term data are lacking. On the basis of the available studies, totally thoracoscopic LAA exclusion does not appear to have poorer outcomes than percutaneous LAAC in terms of stroke prevention.

Effectiveness conclusions

The level and quality of evidence for the evaluation of clinical effectiveness was insufficient to draw a conclusion of non-inferiority of totally thoracoscopic LAA exclusion compared with percutaneous LAA exclusion, perioperatively or over the longer term.

The evidence available for the comparator was of higher quality and was more mature in terms of the number of patients assessed and the duration of follow-up. The small sample sizes and short duration of follow-up in the AtriClip studies impacts on their ability to capture rare events, such as stroke and death. Overall, the findings in relation to effectiveness are less clear than the safety data, although it appears that procedural success rates may be slightly higher for totally thoracoscopic LAA exclusion than for percutaneous LAA exclusion. However the applicant's pre-ESC response contended that given that the mechanism/s for reduction in stroke incidence for both the proposed service and the comparator is by exclusion of the LAA from the systemic circulation and the proposed service has been sufficiently proven to have higher rates of procedural success, as there is no other obvious feasible mechanism for later failure; the lack of evidence on stroke events can be interpreted as a signal of greater effectiveness.

Clinical claim

The ADAR makes a claim of non-inferior safety and non-inferior effectiveness between totally thoracoscopic LAA exclusion and percutaneous LAAC, in which case a cost-minimisation analysis (CMA) would be appropriate. However, non-inferiority is not confirmed for either of these claims due to the lack of direct comparative evidence for the proposed service and comparator, and the poor-quality evidence available for the proposed service, which is largely comprised of single arm, observational studies with inadequate follow-up and high risk of selection and reporting bias.

13. Economic evaluation

The ADAR presents a cost comparison that takes into account the direct procedure-related costs associated with the use of the proposed service and the comparator, with very limited consideration of downstream costs (risk of stroke at 1 year was the only input). A summary of the economic evaluation is provided in Table 4.

Table 4 Summary of the economic evaluation

Component	Description
Perspective	Australian health care
Population	Patients with NVAF who have an absolute contraindication to life-long oral anticoagulation therapy, and at increased risk for thromboembolism based on a CHA_2DS_2-VASc score of ≥2
Prior testing	CT angiography to determine suitability for procedure
Comparator	Percutaneous insertion of a LAA closure device to occlude the LAA
Type of analysis	Cost comparison
Time horizon	1 year
Generation of the base case	Trial based
Software	Excel

CT = computed tomography; LAA = left atrial appendage; NVAF = non-valvular atrial fibrillation

Direct procedure costs for totally thoracoscopic LAA exclusion and percutaneous LAAC are shown in Table 5, based on inputs and costs sourced by the Assessment Group. The total direct cost for the proposed procedure (exclusive of downstream costs) is $21,228, which is $914 more than the comparator procedure ($20,314). This is exclusive of the cost of the thoracoscope and any associated consumables. The Applicant calculated the total direct cost of the proposed procedure ($21,256) to be marginally lower than the cost of the comparator ($21,880).

Table 5 Comparison of procedure costs as re-estimated by the Assessment Group

Procedure Cost Component	Totally thoracoscopic LAA exclusion	Source	Percutaneous LAA closure	Source
MBS fee for LAA occlusion service	$1,698.30	Proposed MBS item	$964.45	MBS item 38276
Associated MBS items (pre-procedural and intra-procedural TOE; anaesthesia)	$1,434.00	MBS item 57352 MBS item 116 MBS item 17615 MBS item 20528 MBS item 22008 MBS item 23035 MBS item 22025 MBS item 22012 MBS item 22051	$1,177.35	MBS item 57352 MBS item 116 MBS item 21941 MBS item 23045 MBS item 22025 MBS item 22012 MBS item 22051
Prosthesis cost	$6,800	Proposed	$11,269.00	Billing Codes BS384, BS332, SI395 (PL, November 2022)
Hospital services	$11,296.00	AR-DRG F09C minus prosthesis cost NHCDC Version 10.0, Round 23, 2018-2019	$6,903.00	AR-DRG F14C minus prosthesis cost NHCDC Version 10.0, Round 23, 2018-2019
TOTAL	**$21,228.30**	**-**	**$20,313.80**	**-**

Source: Derived from ADAR, Section 3B.2, Commentary Tables 14 and 15
AR-DRG = Australian Refined Diagnosis Related Group; LAA = left atrial appendage; MBS = Medicare Benefits Schedule; NHCDC = National Hospital Costs Data Collection (Public); PL = Prostheses List; TOE = transesophageal echocardiography

The applicant's analysis incorporated periprocedural adverse events (major bleeding, systemic embolism, pneumonia, pericarditis, pericardial effusion, cardiac tamponade, death); however, the rates included were not all consistent with the weighted averages calculated in Section 2 of

the ADAR and were not actually applied to any costs in the analysis. Given the uncertainty in the clinical evidence and the very low event rate, the omission of costs to manage periprocedural adverse events is reasonable. However, it may bias results in favour of the proposed service if actual rates of periprocedural adverse events are found to be higher for totally thoracoscopic LAA exclusion than the comparator. The applicant's pre-ESC response acknowledged that absence of evidence on the occurrence of periprocedural adverse events does not equate to evidence of non-occurrence, but contended that the lack of a feasible mechanism of late failure or complications would seem to make more it likely to be the case.

The analysis also included rates of OAC use (warfarin and dabigatran), which may not be appropriate considering the MBS population have an absolute contraindication to lifelong OACs. The applicant's pre-ESC response acknowledged that the ADAR incorrectly used a population with a relative rather than an absolute contraindication to OACs in its modelling. However, the cost of OACs is small compared to the overall cost (average per patient cost of $44 for the proposed service and $237 for the comparator) and so the assumptions used are unlikely to alter decision making.

The only downstream event captured in the cost comparison was the risk of stroke at 1 year (1.54% and 1.71% for the proposed service and comparator, respectively). These rates were not consistent with the clinical evidence presented in the ADAR and their inclusion is not informative.

Device/procedure failure and re-intervention are reasonable inputs for a comparison of two implanted devices; however, follow-up in the clinical studies was insufficient to reliably determine event rates for these outcomes and they were not incorporated in Section 3.

In the absence of evidence to show a significant difference in the risk of stroke after totally thoracoscopic LAA exclusion versus percutaneous LAAC, this input was removed from the analysis by the Assessment Group. The resultant total cost (including anticoagulant use) is $21,272 for totally thoracoscopic LAA exclusion ($21,378 per successful LAA exclusion) and $20,551 for percutaneous LAAC ($21,655 per successful LAAC). The applicant's estimate was $21,841 per successful LAA exclusion for the proposed intervention versus $23,811 per successful LAAC for the comparator intervention.

14. Financial/budgetary impacts

A market share approach was adopted to inform the utilisation estimates and financial implications to the Government upon MBS listing of the proposed service. The basis for the projected number of patients/procedures was historical data for services relating to MBS item 38276 (Figure 1) and the Applicant's assumption regarding uptake and market share.

Table 6 shows the estimated uptake and cost to the MBS of the proposed service, calculated by the Assessment Group. The 75% benefit is used for all costs.

Table 6 Estimated uptake of totally thoracoscopic LAA exclusion using market share approach

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5
Number of services for percutaneous LAAC (total market)	613	675	742	817	898
Market share assumption - TT LAA exclusion	8%	13%	26%	30%	30%
Number of services for TT LAA exclusion (shared market)	49	88	193	245	269
Number of services for percutaneous LAAC (shared market)	564	587	549	572	629
Total MBS cost of TT LAA exclusion services	$62,513	$111,741	$245,831	$312,016	$343,218
Total MBS cost of services associated with the TT LAA exclusion services	$52,788	$94,358	$207,588	$263,477	$289,825

Source: Derived from ADAR, Section 4.2, Commentary Tables 16 and 17, and Section 4.3, Commentary Table 18
LAA = left atrial appendage; LAAC = left atrial appendage closure; MBS = Medicare Benefits Scheme; TT = totally thoracoscopic

Although the estimates have been based entirely on a market share approach, it is possible that the proposed service may grow the market because patients who were unsuitable for percutaneous LAAC due to LAA size or morphology may be suitable for totally thoracoscopic LAA exclusion. The Applicant refers to "10-20% patients for whom percutaneous occlusion of the LAA is not viable due their anatomy, or, as the percutaneous occlusion device requires some post implant period of anti-platelet therapy, their absolute contraindication to receiving any anti-coagulation therapy". This equates to an additional 70 to 120 patients in the first year of listing (not incorporated in the estimates).Table 7 shows the estimated net cost to the MBS if the proposed service is listed. The estimates consider all MBS costs listed in Table 5. Costs related to the treatment of perioperative complications and longer-term outcomes are not included because event rates are uncertain. Sensitivity analyses showed that matching the proposed fee for totally thoracoscopic LAA exclusion with the comparator fee has the largest impact on MBS costs.

Table 7 Net cost to the MBS of the proposed listing

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5
Current scenario – no MBS listing for TT LAA exclusion					
Total MBS cost of percutaneous LAAC procedures	$985,509	$1,084,060	$1,192,466	$1,311,712	$1,442,884
Proposed scenario – MBS listing for TT LAA exclusion					
Total MBS cost of percutaneous LAAC services	$906,668	$943,132	$882,425	$918,199	$1,010,018
Total MBS cost of TT LAA exclusion services	$115,300	$206,100	$453,419	$575,493	$633,043
Total MBS cost of proposed listing	$1,021,969	$1,149,232	$1,335,844	$1,493,692	$1,643,061
Net Cost					
Net cost to MBS of proposed listing	$36,460	$65,172	$143,378	$181,980	$200,178

Source: ADAR, Section 4.4, Commentary Tables 19
LAA = left atrial appendage; LAAC = left atrial appendage closure; MBS = Medicare Benefits Scheme; TT = totally thoracoscopic

The ADAR has not addressed out of pocket costs and no information was provided on the management of patients who cannot receive the proposed or comparator device at the time of the implantation procedure.

It is anticipated there will be a reduction in costs to the PBS associated with reduced use of antiplatelet therapy due to a reduction in percutaneous LAAC procedures.

Savings to the PL are also anticipated considering that the proposed cost for the AtriClip PRO2 ($6,800) is lower than the benefit for comparator percutaneous LAAC devices ($11,269). Table 1 shows the estimated net cost to the PL if the proposed service is listed on the MBS and the PL benefit is $6,800.

Table 1 Net cost to the PL of the proposed MBS listing

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5
Current scenario – no MBS listing for TT LAA exclusion					
Total PL cost of percutaneous LAAC procedures	$6,913,193	$7,604,513	$8,364,964	$9,201,460	$10,121,607
Proposed scenario – MBS listing for TT LAA exclusion					
Total PL cost of percutaneous LAAC services	$6,360,138	$6,615,926	$6,190,073	$6,441,022	$7,085,125
Total PL cost of TT LAA exclusion services	$333,728	$596,538	$1,312,384	$1,665,718	$1,832,290
Total PL cost of proposed listing	$6,693,866	$7,212,464	$7,502,457	$8,106,741	$8,917,415
Net Cost					
Net cost (saving) to PL of proposed listing	-$219,328	-$392,048	-$862,507	-$1,094,720	-$1,204,192

Source: ADAR, Section 4.5, Commentary Tables 20
LAA = left atrial appendage; LAAC = left atrial appendage closure; MBS = Medicare Benefits Scheme; PL = Prostheses List; TT = totally thoracoscopic

While the full estimates are not displayed here, the net cost of hospitalisation if the proposed service is listed on the MBS increases from $215,598 in Year 1 to $1,183,713 in Year 5, excluding hospitalisations for managing periprocedural or downstream complications or device failures/revisions.

15. Other relevant information

PASC noted there may be barriers to access to the proposed service for people in rural and remote areas.

16. Key issues from ESC to MSAC

Main issues for MSAC consideration

Item Descriptor issues:

- The applicant has agreed to reduce the proposed fee for the service so that it is the same as MBS item 38276.
- The MBS item descriptor or Explanatory Note for the proposed service should specify that provision of the service is restricted to cardiothoracic surgeons with training in video-assisted thoracoscopic surgery. Further input from the relevant professional body should be sought.

Clinical issues:

- The clinical need for the proposed service is unclear. There are transcatheter devices listed on the PL that largely address the clinical need using a minimally invasive technique – only a very small group of patients (unable to take dual anti-platelet therapy and with an absolute contraindication to oral anticoagulant therapy) would have a clinical need for totally thoracoscopic LAA; and the size of this patient population is not well defined.
- Inappropriate methods for comparison have been used. Data have been pooled for naïve indirect comparison with no consideration of study quality.
- The clinical claims of non-inferior safety and non-inferior effectiveness are not confirmed. The body of evidence for standalone totally thoracoscopic LAA exclusion largely comprises small, retrospective observational studies with heterogeneous eligibility requirements, undefined outcome measures, inadequate follow-up, and risk of selection and reporting bias.

Economic issues:

- The economic findings are based on limited data and present a cost comparison analysis. Given that the clinical claims of non-inferior safety and effectiveness are not supported, this approach is not recommended by the MSAC Guidelines.
- The cost comparison does not consider periprocedural complications, nor does it adequately consider downstream costs. Robust clinical data to support these inputs are lacking.

Financial issues:

- The financial analysis is based on a market-share approach and uptake of the proposed service will likely be restricted due to limitations in the number of cardiothoracic surgeons and centres that can perform this procedure.
- Use of the service outside the proposed patient population is unlikely given it is the same population currently eligible for percutaneous LAA closure and the patient's absolute contraindication to lifelong oral anticoagulation must be documented by an independent medical practitioner.
- The MBS listing could potentially expand the market as the proposed service would provide an option for 10–20% of patients who, according to the applicant, are eligible for percutaneous LAAC but are unsuitable due to LAA size or morphology. Sensitivity analysis suggests that the financial impact could increase along with this growth in the market.
- The cost of the AtriClip PRO2 LAA Exclusion System is substantially higher than the PL benefit for the AtriClip FLEX LAA Exclusion System, which is indicated for open occlusion of the LAA.
- The ADAR did not address out-of-pocket costs, which may be significant due to the specialised nature of the procedure and the small number of providers available.

ESC discussion

ESC noted that this application from AtriCure is requesting Medicare Benefits Schedule (MBS) listing of totally thoracoscopic implantation of an epicardial clip (AtriClip) to exclude the left atrial appendage (LAA) for patients with non-valvular atrial fibrillation (NVAF) who have an absolute contraindication to oral anticoagulation (OAC).

MSAC has not previously considered totally thoracoscopic LAA exclusion in NVAF patients, but it has previously considered percutaneous LAA closure (LAAC) for patients with NVAF. At its meeting in July 2016, MSAC supported listing of percutaneous LAAC (MBS item 38276), and at its March/April 2021 meeting, MSAC supported an amendment to expand the list of absolute contraindications to oral anticoagulation therapy.

This application is for a new MBS item that would be a replacement or alternative to current MBS item 38276 (transcatheter occlusion of the LAA). ESC also noted that the applicant is currently preparing a separate applicant-developed assessment report (ADAR) for LAA exclusion in patients undergoing open cardiac surgery (MSAC Application 1666).

ESC noted that feedback from the Australian and New Zealand Society of Vascular Surgery (ANZSVS) was generally supportive of the thoracoscopic LAA exclusion procedure but was not supportive of a higher fee compared with percutaneous LAA (as originally proposed in the ADAR). ESC noted that feedback from Hearts4Heart was also supportive, stating that the procedure improves management of patients at high risk for standard therapies and those who cannot tolerate blood thinning medications.

ESC considered that the original proposed MBS fee required additional justification as it was substantially higher than the comparator service, despite having similar total procedure times and similar investment in time to undertake extensive training for left atrial appendage (LAA) occlusion. However ESC noted that this issue was now resolved as in its pre-ESC response, the applicant revised the proposed fee so that it was the same as the comparator procedure (i.e. from $1,698.30 to $964.45),

The applicant also proposed further amendments to the item descriptor in response to several issues raised by the commentary. These amendments include adding the words “for stroke prevention” in the item descriptor, to match the PICO intervention description and removing the inappropriate MBS item exclusions, which had been included to align the descriptor and explanatory notes with those for the transcatheter appendage closure device.

ESC considered that due to the complexity of the procedure and training required, that it would be necessary to specify that the service must be provided by cardiothoracic surgeons with training in video-assisted thoracoscopic surgery. ESC noted that in its pre-ESC response, the applicant agreed with this proposal. ESC considered that advice should be sought from the relevant professional body on the training that is required to perform this procedure, ESC also noted that while the clinical evidence presented in the ADAR was restricted to standalone totally thoracoscopic LAA exclusion, the proposed MBS item descriptor allows for concomitant procedures. ESC noted that up to 30% of totally thoracoscopic LAA exclusion procedures could be performed alongside radiofrequency ablation or mini-thoracotomy valve surgery.

ESC noted that the proposed item descriptor had a lifetime restriction of once per patient. While ESC considered this was appropriate, ESC questioned what would happen in the case of a requirement to reposition or remove the device and noted that no evidence was presented around this. ESC considered that while this element should align with the percutaneous LAAC process, ESC also questioned whether repositioning of the device could be undertaken without open surgery; ESC considered that advice should be sought from a professional body on how this would occur, and noted that information on the likelihood of repositioning or removal is important for patient informed consent.

ESC considered that the descriptor for MBS item 38276 should also be modified as there are currently no restrictions on which providers undertake this service, though ESC noted that typically the service would be undertaken by interventional cardiologists, electrophysiologists or cardiothoracic surgeons who have training in the transcatheter occlusion of the LAA.

ESC noted the clinical management algorithm and considered the clinical need for the intervention. ESC noted that the comparator – transcatheter occlusion of left atrial appendage – largely addresses the clinical need for the majority of patients using a minimally invasive technique, and using transcatheter devices (WATCHMAN and WATCHMAN FLX from Boston Scientific and Amplatzer Amulet from Abbott Medical) that are included on the Protheses List (PL). ESC therefore considered that the clinical need for the proposed service is unclear as the group of patients who have a clinical need for totally thoracoscopic LAA exclusion – i.e., those who are unable to receive dual antiplatelet agents with an absolute contraindication to OAC therapy and having minimally invasive valve surgery – would be very small even after taking into account those patients who have an absolute contraindication to OAC and who are also unsuitable for percutaneous LAAC due to LAA size and morphology. ESC considered additional evidence to confirm the patient population eligible for the intervention would be useful.

ESC noted that the body of evidence for standalone totally thoracoscopic LAA exclusion largely comprises small, retrospective observational studies with heterogenous eligibility requirements, undefined outcome measures, inadequate follow-up and a high risk of selection and reporting bias. ESC noted that 3 out of the 11 identified studies relating to totally thoracoscopic LAA exclusion restricted eligibility to patients with NVAF, of which only one study (45 patients) explicitly mentioned that patients had an absolute contraindication to OAC therapy as per the population of interest.

Conversely, ESC noted that the evidence for the comparator included multicentre, randomised controlled trials, with all studies having a low or medium risk of bias. ESC further noted that data were pooled in a naïve indirect comparison with no consideration of study quality.

Regarding comparative safety, ESC noted that the ADAR presented weighted means for the single arm studies with non-inferiority testing using a margin of 5%, which was not justified. ESC noted that, overall, the totally thoracoscopic LAA exclusion studies showed a larger range in rates of all perioperative adverse events (from 0% to 26%) compared with the comparator studies (from 2.2% to 2.8%). ESC considered this understandable given that the totally thoracoscopic surgical approach is more invasive than the percutaneous approach. ESC also noted that two of the intervention studies reported pericarditis (rates of 6.7% and 10.7%), while pericarditis was not reported in any of the comparator studies. However, pericardial effusion was reported in all three comparator studies and had a numerically higher rate (ranging from 1.9% to 5.2%) compared with the one intervention study that specifically reported this outcome (1.8%). Overall, ESC considered the comparative safety findings to be highly uncertain given the heterogeneity across the studies for patient characteristics and study design.

Regarding comparative effectiveness, ESC noted that procedural success ranged from 99.4% to 100% across the intervention studies, appearing to be higher than that of the comparator studies (94.7% to 95.1%). However, “procedural success” was not defined in the ADAR. ESC also noted that while totally thoracoscopic LAA exclusion does not appear to have poorer outcomes than percutaneous LAAC in terms of stroke prevention, the number of stroke events was low across all studies, and long-term data are lacking. Similar to the comparative safety data, ESC noted that the reporting of clinical effectiveness data was generally poor due to the large majority of studies being small, low level and observational, with insufficient follow-up.

ESC considered that the clinical claim of non-inferior safety and non-inferior effectiveness is not confirmed. This is due to a lack of direct comparative evidence for the proposed service and comparator, and the poor-quality evidence available for the proposed service, which largely

comprises single-arm, observational studies with inadequate follow-up and a high risk of selection and reporting bias.

ESC noted that the commentary identified several issues with the economic evaluation. Based on an assumption of non-inferior safety and non-inferior effectiveness between totally thoracoscopic LAA exclusion and percutaneous LAAC, the applicant claimed to have provided a cost-minimisation analysis. However, ESC noted that the applicant provided a cost comparison analysis of treatment costs for the intervention and comparator over a one-year period. The cost comparison captured risk of stroke at 1 year, which was the only input for downstream costs. This was based on data from single arm studies that were underpowered for this outcome, with very few events reported. ESC noted that, according to the 2021 MSAC Guidelines (p. 203), a cost analysis is only considered acceptable in cases where "the proposed health technology is demonstrated to be no worse in terms of effectiveness but has a superior safety profile compared with the comparator". ESC considered that given that this clinical claim was not supported, the use of this form of analysis may be inappropriate.

ESC noted that the ADAR reported the total costs to provide the service over 1 year to be $21,733 ($21,841 per successful LAA exclusion) for the intervention and $22,597 ($23,811 per successful LAA exclusion) for the comparator. The commentary recalculated these values to be $21,272 for the intervention and $20,551 for the comparator. However, ESC noted that neither the applicant nor the commentary used the lower fee agreed to in the pre-ESC response. ESC noted that the key drivers of the cost were prostheses costs (particularly for the comparator) and hospital costs (particularly for the intervention). No sensitivity analyses were conducted.

ESC noted the following additional limitations of the economic evaluation, which may bias results or lead to questions around the reliability of the results:

- exclusion of costs of peri-procedural adverse events;
- inconsistencies in the rates of ischaemic and haemorrhagic stroke compared with the clinical evidence in the ADAR;
- potential underestimation of true costs due to the discounting process
- the assumption that 50% of NVAF patients are on warfarin as opposed to a direct OAC.

ESC considered that the results of the cost comparison analysis were not informative due to the issues with the clinical claim of non-inferior safety and effectiveness and additional limitations identified.

Regarding the financial impact of the intervention, ESC noted that a market share approach was used to inform utilisation estimates. The estimated usage is 40 patients in year 1, increasing to 242 patients in year 6. ESC noted as per the commentary that the estimates are based on a population with an overall contraindication to lifelong OAC rather than an absolute contraindication. However, ESC considered that use of the service outside of the proposed population is unlikely given it is the same population currently eligible for percutaneous LAA closure and the patient's absolute contraindication to lifelong OAC must be documented by an independent medical practitioner.

ESC noted that the sensitivity analyses around financial impacts provided in the commentary included the proposed MBS item fee being the same as the comparator – ESC considered that this is now the base case as the applicant has agreed to reduce the proposed fee to the fee for the comparator. ESC noted that, according to the applicant, the market share for the proposed service could grow by 10–20% due to patients being eligible for percutaneous LAAC but unsuitable due to LAA size or morphology. ESC noted that, if the market share does increase over time, the budget impact increases significantly, from $45,575 in year 1 to $266,904 in year 6.

ESC noted that it is anticipated there will be a reduction in costs to the Pharmaceutical Benefits Scheme associated with reduced use of antiplatelet therapy. Savings to the PL are also anticipated, given that the proposed cost for the AtriClip device ($6,800) is lower than the benefit for the comparator devices ($11,269). However, ESC noted that the cost of the AtriClip PRO2 LAA Exclusion System is substantially higher than the PL benefit for the AtriClip FLEX LAA Exclusion System, which is indicated for open occlusion of the LAA. This significant price difference was not justified.

ESC noted that the ADAR did not address out-of-pocket costs, which ESC considered may be significant due to the specialised nature of the procedure and the small number of providers available. ESC considered that to address this, informed financial consent (which may be facilitated by providing cost comparisons with percutaneous LAAC) must be obtained before undertaking any procedure.

17. Applicant comments on MSAC's Public Summary Document

The applicant did not offer a comment on the Public Summary Document.

18. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website: visit the MSAC website.