

# Medical Services Advisory Committee (MSAC) Public Summary Document

## *Application No. 1772 – Single-chamber leadless pacing with atrioventricular synchronous pacing in patients with bradycardia*

**Applicant:** Medtronic Australasia Pty Ltd

**Date of MSAC consideration:** 3-4 April 2025

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 a new Medicare Benefits Schedule (MBS) listing for the insertion of a single-chamber leadless pacemaker (LPM) with atrioventricular (AV) synchronous pacing (Micra™ AV) for patients with bradycardia due to AV block who are in sinus rhythm was received from the medical device company Medtronic Australasia Pty Ltd by the Department of Health. This submission to MSAC was lodged to facilitate public funding through the MBS for insertion of a LPM and listing of the Micra AV LPM on the Prescribed List of Medical Devices and Human Tissue Products (PL). The applicant intends to apply for PL listing of the Micra AV device at the proposed benefit of \$redacted following MSAC consideration.

### 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 the creation of new items for the insertion of a single-chamber leadless pacemaker (LPM) with atrioventricular (AV) synchronous pacing (Micra AV™) for patients with bradycardia due to AV block who are in sinus rhythm. MSAC considered that the current MBS items for insertion, retrieval, replacement, and explantation could be utilised with amendments to include the target population for the Micra AV. MSAC noted that there was no current application to list the Micra AV on the Prescribed List of Medical Devices and Human Tissue Products (PL) but noted the applicant's stated intent to apply to the PL under the Tier 3 PL application pathway following MSAC consideration of the comparative safety, clinical effectiveness, and cost-effectiveness of the device. MSAC noted that there was no clinical or economic comparison between the Micra AV and the currently PL-listed Micra VR LPM. MSAC advised the Medical Devices and Human Tissue Advisory Committee (MDHTAC) that due to the absence of comparative data, there was no evidence to support the higher proposed PL benefit for the Micra AV over the Micra VR. MSAC considered that despite the low-certainty evidence for comparative safety, Micra AV was likely to be superior in safety in terms of some complications (e.g. lead and pocket complications) and risk of reinterventions when compared to conventional transvenous pacemakers (TVPM). MSAC considered that there were likely quality-of-life benefits following implantation of an LPM compared with a conventional pacemaker with leads, despite limited evidence for the proposed population. MSAC noted that any resubmission to MSAC requesting a higher PL benefit would require new evidence comparing the effectiveness of the Micra AV with comparable leadless and leaded pacemakers, and advice from clinical experts in the Medical Devices and Human Tissue Advisory Committee's

Cardiovascular Expert Clinical Advisory Group on the appropriate population and comparative clinical assessment.

### Consumer summary

This application from Medtronic Australasia Pty Ltd requested listing of the Micra™ AV, a single-chamber leadless pacemaker (LPM) with atrioventricular (AV) synchronous pacing, on the Prescribed List. The application also requested a new Medicare Benefits Schedule (MBS) item for the insertion of the pacemaker in patients who have a slow heart rate (called bradycardia) because of a particular heart disorder (called atrioventricular block) but have a normal heart rhythm that beats regularly (called sinus rhythm). The human heart consists of four chambers, which includes two upper and two lower chambers. An electrical signal starts in the top right chamber of the heart (right atrium) and spreads downwards, telling the rest of the heart when to beat. In atrioventricular block, the electrical signals from the top chambers of the heart are blocked from transmitting to the lower chambers of the heart (ventricles), which leads to a slow heart rate.

The Micra AV is a pacemaker, which is a medical device that sends a signal to the heart to help it beat at the right rate and rhythm. Traditional pacemakers are inserted in the chest, in a pocket in the tissue just below the collarbone. These traditional pacemakers have leads that run from the chest pocket to the heart through a vein. The Micra AV is different to these pacemakers because it is inserted directly into the heart and does not have any leads. The Micra AV has technology that mimics the natural beating of the heart, by timing the beating of the top and lower chambers of the heart, so that they are in sync. This technology detects when the top chamber of the heart on the right side (right atrium) has sent an electrical signal and done a beat. Directly after, the device will send a signal to the bottom chamber of the heart on the right side (right ventricle) to beat. This makes sure that the right atrium beats before the right ventricle. This is so that the blood from the right atrium has time to flow down into the right ventricle. This blood can then be sent to the lungs to have oxygen added to it and from there, the oxygenated blood is sent to the rest of the body.

MSAC noted that the Micra AV's battery cannot be replaced. At the end of its battery life the Micra AV is not usually removed, and it remains in place in the heart (in the right ventricle) but is deactivated. A new Micra AV is then inserted into the right ventricle, next to the old one. Removal of the Micra AV once it has been in place for a while can be difficult. It is estimated that up to three Micra devices can fit in the heart and the estimated battery life of the Micra AV is 16 years.

MSAC concluded that, for some patients, there is a need for pacemakers that do not have leads, like the Micra AV. For example, in some patients whose veins are hard to access or who have a high risk of infection affecting the leads and chest pocket.

Based on the evidence, MSAC concluded that the Micra AV is most likely to be safe. However, MSAC concluded that the evidence about the effectiveness and value for money of the Micra AV compared with a traditional pacemaker that has leads was highly uncertain. MSAC also noted that there was no evidence provided about the effectiveness and value for money of the Micra AV compared with a different pacemaker that also has no leads but does not have the ability to synchronise the beating of the top and lower chambers of the heart (called the Micra™ VR). The Micra VR is already funded and listed on the Prescribed List.

MSAC noted that the Micra AV has the potential to replace or be used in place of the Micra VR in some patients. However, it would not be suitable for younger, relatively fit patients, as it does not have the ability to synchronise the beating of the atrium and ventricle 100% of the time. It can only provide synchronous beating of the heart reliably when the heart beats less than 100 beats per minute. Which means that active and younger patients might not be suitable for the Micra AV because they are likely to be more active, which will raise their heartbeat above 100 beats per minute when they are moving around.

### Consumer summary

Because of the lack of evidence comparing the Micra AV with the Micra VR, MSAC did not support the request for a higher fee for the Micra AV as MSAC could not determine if the Micra AV was safer, more effective or better value for money than the Micra VR.

MSAC also concluded that a new MBS item number was not needed for insertion of the Micra AV and that instead the current MBS item for insertion of pacemakers that do not have leads ([MBS item 38372](#)) could be used. MSAC suggested that advice could be added to the MBS item notes to make it clear which patients the Micra AV is useful for.

#### **MSAC's advice to the Commonwealth Minister for Health and Aged Care**

MSAC did not support the creation of new items for the insertion of Micra AV in patients with bradycardia due to AV block who are in sinus rhythm. MSAC advised that existing MBS items for leadless pacemakers (for insertion, retrieval, replacement, and removal of leadless pacemakers) could be used instead. The existing MBS items would need explanatory notes added to them, to include the people eligible for the Micra AV.

MSAC considered the device likely to be safer than traditional pacemakers with leads, particularly for patients with limited vein access and/or a high risk of infection. While the Micra AV may offer quality-of-life benefits, MSAC concluded that the Micra AV may perform the same as (but not better than) traditional lead-based pacemakers and the already-listed leadless Micra VR, which lacks the AV synchronisation feature.

MSAC advised the Medical Devices and Human Tissue Advisory Committee (MDHTAC) that, in the absence of comparative clinical data for the Micra AV over the already PL listed Micra VR, a higher proposed PL benefit for the Micra AV could not be justified.

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

MSAC noted this application from Medtronic Australasia Pty Ltd was to facilitate the application for listing of a single-chamber leadless pacemaker (LPM) with rate-responsive atrioventricular (AV) synchronous pacing (Micra™ AV) to the right ventricle on the Prescribed List of Medical Devices and Human Tissue Products (PL) via the Tier 3 full health technology assessment (HTA) pathway. MSAC also noted the application requested a new Medicare Benefits Schedule (MBS) item for the insertion of the Micra AV for patients with bradycardia due to AV block who are in sinus rhythm. MSAC considered it appropriate that Micra AV insertion be performed as an inpatient service, in public or private hospitals, within a cardiac catheterisation laboratory or operating room, and to be performed by specialist cardiologists (interventional cardiologists and cardiac electrophysiologists) or cardiac surgeons.

MSAC considered that there was a clinical need for LPMs, including the Micra AV, as some patients are not suitable for conventional transvenous pacemakers which include leads, due to limited venous access and/or a high risk of lead or pocket infection. MSAC noted that unlike transvenous pacemakers, LPMs do not require a subcutaneous generator pocket, reducing the risk of pocket infection or haematoma compared with transvenous pacemakers. MSAC also noted that LPMs eliminate complications associated with leads, such as lead dislodgement and lead fracture. The clinical benefits of LPMs were previously noted in [MSAC Application 1672](#), which evaluated the insertion and removal of leadless pacemakers in the context of the Micra™ VR, a single-chamber LPM with ventricular pacing but without the ability for AV synchronous pacing. MSAC noted that the Micra VR is currently used for patients for whom there are concerns about venous access and risk of infection.

MSAC noted that the Micra AV senses the right atrium and ventricle, but only paces the right ventricle - similar to the functionality of a VDD pacemaker. Therefore, although the Micra AV has

dual chamber functionality it was classified as a single-chamber device because it only paces the ventricle and has no atrial lead.

MSAC noted that the algorithm was based on joint guidance from the American College of Cardiology, American Heart Association and Heart Rhythm Society, coupled with the algorithm in MSAC Application 1672. MSAC Application 1672 was for MBS listing of services associated with the use of a LPM for treating bradyarrhythmia indicated for single-chamber ventricular pacing. The clinical management algorithm for MSAC Application 1672<sup>1</sup> was based on local expert advice, with Australian clinicians referring to the 2018 ACC/AHA/HRS guidelines<sup>2</sup> due to the absence of Australian-specific bradycardia management algorithms. In comparing the clinical management algorithms from [Application 1672](#) and this application, MSAC considered that the proposal in the application of the Micra AV will likely lead to it replacing the Micra VR as an option for patients without permanent AF as it enables AV synchronous pacing. MSAC noted the applicant stated this was a consequence of the Micra VR being the only available LPM at the time of MSAC Application 1672, and therefore the only leadless option for patients contraindicated for transvenous leads. However, MSAC noted local expert advice that the Micra VR was infrequently used in patients without AF (<5%).

MSAC noted that the primary comparator for insertion of the Micra AV was insertion of a conventional dual-chamber transvenous pacemaker (DC-TVPM). MSAC noted the applicant's pre-MSAC response, which reiterated that the Micra VR was neither a relevant clinical comparator for the Micra AV nor relevant for the purpose of PL benefit setting. However, MSAC considered the Micra VR to be an appropriate secondary comparator due to the Micra AV replacing the Micra VR as an option for patients with bradycardia due to paroxysmal or permanent high-grade AV block (without permanent AF) and being proposed at a higher PL benefit (\$redacted) than for the Micra VR (\$10,083).

MSAC noted that the main source of clinical evidence was a large, non-randomised cohort study – the Micra AV Coverage with Evidence Development (CED) study. MSAC noted this study had a 24-month follow up period, was based on United States claims data and involved 118,110 patients who had either a Micra AV or DC-TVPM inserted. MSAC noted that propensity score overlap weightings were used to construct a weighted cohort of patients differentiated by pacemaker type (Micra AV or DC-TVPM). MSAC noted that no clinical comparison of the Micra AV and Micra VR was presented. As the Micra AV CED study did not capture data on quality of life (QoL), AV synchrony or battery life, MSAC noted that 5 additional studies were included as supportive evidence: 2 single-arm studies and 1 modelling study on the Micra AV or AV2 for data on battery life and AV synchronicity, and 2 prospective non-randomised studies comparing Micra VR with conventional pacemakers for QoL outcomes.

MSAC considered the clinical claim of superior safety for the Micra AV compared with standard DC-TVPMs was supported, based on data from the CED study. MSAC noted that reported outcomes included lower risks of acute complications, chronic complications and reinterventions in patients who had a Micra AV inserted. MSAC considered that despite the low-certainty evidence for comparative safety, Micra AV was likely to be superior in safety than conventional TVPMs in terms of some complications (e.g. lead and pocket complications) and the risk of reintervention

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<sup>1</sup> MSAC Application 1672: [Ratified PICO Confirmation](https://www.msac.gov.au/sites/default/files/documents/1672%2520Ratified%2520PICO.pdf),  
<https://www.msac.gov.au/sites/default/files/documents/1672%2520Ratified%2520PICO.pdf>

<sup>2</sup> Kusumoto, FM, et al. 2019, '2018 ACC/AHA/HRS guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay. A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society', *Circulation*, vol. 140, no. 8, pp. e382-e482.

MSAC noted the clinical claim of non-inferior effectiveness of the Micra AV compared with standard DC-TVPMs, based on data from the CED study, specifically with regard to all-cause mortality. MSAC noted that the study showed a statistically significant higher risk of all-cause mortality for those who had a Micra AV inserted compared to those who had a DC-TVPM inserted (hazard ratio = 1.55; 95% CI = 1.44 to 1.68). However, MSAC considered that this finding was likely due to selection bias, because those who were contraindicated to have a DC-TVPM inserted, and thus had a Micra AV inserted, were likely to have a higher co-morbidity burden and have a poorer prognosis in general. MSAC considered that this bias could not be overcome by the use of the propensity score overlap weights. MSAC noted, that because of survival bias, this was likely to result in biased observations regarding the relative frequency of complications that the applicant used to populate the economic model.

MSAC noted the clinical claim of inferior technical performance of the Micra AV compared to standard DC-TVPMs, specifically in relation to AV synchrony, while all other technical performance variables were expected to be non-inferior. MSAC considered the Micra AV's reduced capacity for AV synchrony compared with DC-TVPMs to be a limitation. MSAC noted that with optimal programming, the Micra AV achieved resting AV synchronicity of 84.1% and ambulatory AV synchronicity of 82.6%. However, MSAC considered that the Micra AV's ability for AV synchronicity was likely to improve with technological advancements, noting that the Micra AV2 demonstrated better synchrony than the Micra AV1.

MSAC concluded that the clinical effectiveness of the Micra AV remains uncertain. MSAC considered that evidence for the clinical effectiveness of the Micra AV compared with DC-TVPMs presented was limited however, acknowledged potential quality-of-life benefits associated with LPM implantation compared to conventional pacemaker with leads, despite limited evidence for the proposed population.

MSAC noted the applicant provided a revised economic model in the pre-MSAC response which took a lifetime time horizon instead of the previous 16-year time horizon and included replacement costs for DC-TVPMs after 11 years and the Micra AV after 16 years, to address the issues identified by the evaluation sub-committee (ESC). The revised model estimated the incremental cost-effectiveness ratio (ICER) at \$redacted/quality-adjusted life year (QALY) gained, compared to ICER \$redacted/QALY gained in the previous revised model provided to ESC. MSAC considered that although the revised model was not able to be fully evaluated prior to MSAC consideration, it was likely that significant limitations remained which favoured the Micra AV. These limitations included (in addition to the potential bias affecting clinical outcomes outlined above):

- the model included replacement costs for both the Micra AV and DC-TVPMs at their estimated battery life end, but did not model the Micra AV being replaced with an alternative pacing system,
- the model did not consider replacement costs in the first 2 years, despite the replacement rate of Micra AV is 5 times that of DC-TVPM,
- the modelled anaesthesia costs of the procedures were for 2 hours for DC-TVPMs and 45 minutes for LPMs, whereas the expected duration for both procedures is 30 minutes,
- there were no sensitivity analyses for the revised model, such as those to test different time horizons and the assumptions made about key drivers of the model (for example, QoL, time, disutilities for procedures, and infection costs).

Therefore, MSAC concluded that the evidence about cost-effectiveness was uncertain.

Consistent with PASC and ESC, MSAC considered the Micra VR should have been included as a relevant secondary comparator. Therefore, the potential impact of the Micra AV on the Micra VR's market share should be evaluated.

MSAC noted the revised financial impact of the proposed listing of the Micra AV for the MBS was a saving of \$redacted in year 1 and \$redacted in year 6. However, MSAC noted that for the Australian healthcare system overall due to higher prosthesis costs, resulting in a cost of \$redacted in year 1 and \$redacted in year 6. MSAC noted these estimates, which have not been independently evaluated, were similar to those presented to ESC, but MSAC considered these to still to be uncertain due to the unassessed impact on Micra VR's market share.

Overall, MSAC did not support the creation of new items for the insertion of Micra AV. Instead, MSAC advised that existing MBS items 38372, 38373, 38374 and 38375, which cover insertion, retrieval, replacement, and explantation could be utilised, with explanatory notes regarding the device to include the target population for the Micra AV. MSAC considered that advice from the experts on the Cardiovascular Expert Clinical Advisory Group (CVECAG) would help inform amendments to the explanatory notes regarding the appropriate population. MSAC also noted that the anaesthesia initiation item and average anaesthesia time for insertion for both Micra AV and the Micra VR would be the same.

MSAC advised the MDHTAC there was no justification for the higher proposed PL benefit for the Micra AV. There was an absence of comparative data between the Micra AV and Micra VR to allow for the assessment of the relative cost-effectiveness of the proposed higher PL benefit for Micra AV compared to the current PL benefit for Micra VR (\$10,083). MSAC considered that a re-application proposing a higher PL benefit for the Micra AV would require advice from MDHTAC and the CVECAG of MDHTAC on the appropriate population and include clinical and economic evidence to support the higher PL benefit.

## **4. Background**

MSAC has not previously considered single-chamber LPM with AV synchronous pacing (Micra AV) for patients with bradycardia due to AV block who are in sinus rhythm. However, MSAC recently supported MBS funding for the insertion, retrieval, replacement and explanation of Medtronic's leadless single-chamber ventricular pacemaker (Micra VR) for bradycardia at the July 2022 meeting (MSAC Application 1672). The services associated with the Micra VR device were subsequently listed on the MBS in November 2023 (MBS items 38372, 38373, 38374 and 38375). The same MBS items are proposed by the applicant to be used for the Micra AV device.

The Micra VR was listed on the PL in November 2023 (billing code MI516) at a benefit of \$10,083 (Grouping 08.04.04). Two other single-chamber LPMs, the Micra VR2 (Medtronic) and the Aveir VR (Abbott Medical Australia Pty Ltd), were also listed on the PL in November 2024.

## **5. Prerequisites to implementation of any funding advice**

The Micra AV LPM is included on the Australian Register of Therapeutic Goods (ARTG) along with an 'introducer' for inserting the device. Table 1 provides details of the Therapeutic Goods Administration status from the ARTG for the Micra AV and its consumables.

**Table 1 Micra AV LPM and consumables listed on the ARTG**

<b>Product name (sponsor)</b>	<b>ARTG summary</b>	<b>Functional description</b>	<b>Intended purpose</b>
Micra AV MC1AVR1 Intracardiac pacemaker (Medtronic Australasia Pty Ltd)	<b>ARTG ID:</b> 391832, 391833 <b>Start date:</b> 5/07/2022 <b>Category:</b> Medical Device Class III <b>GMDN:</b> 60789 Intracardiac pacemaker	MR Conditional single-chamber, transcatheter pacing system with SureScan technology is a programmable cardiac device that monitors and regulates the patient's heart rate by providing rate-responsive bradycardia pacing to the right ventricle and AV synchrony based on the mechanical sensing of atrial activity. The device senses both the electrical activity and the mechanical activity of the patient's heart using sensing and pacing electrodes and an accelerometer enclosed in a titanium capsule.	<p>Transcatheter pacing systems are sterile, single use only, active implantable medical devices that are implanted in patients by healthcare professionals trained in cardiology. Transcatheter pacing systems are intended to improve cardiac output, prevent symptoms of and protect against arrhythmias related to cardiac impulse formation or conduction disorders by providing pacing therapy to the heart. Micra AV Model MC1AVR1 is indicated for VDD pacing in patients when a dual-chamber transvenous pacing system is considered a poor option or not deemed necessary for effective therapy, and when a right ventricular transcatheter pacing system promoting AV synchrony at rest is acceptable. Conditions when a patient is considered a poor candidate for transvenous pacing may include, but are not limited to, tortuous anatomy, a need to preserve venous access, or increased risk of infection. The device provides AV synchrony at rest and rate-responsive (VVIR) pacing during periods of high patient activity. Device-mediated AV synchrony can vary depending on patient condition and activity levels, and it can be limited at high sinus rates. During periods of intermittent AV synchrony, the device will provide ventricular pacing support with an increased potential for pacing rate variability. Micra AV Model MC1AVR1 is indicated for use in patients who have experienced one of the following:</p> <ul style="list-style-type: none"> <li>- paroxysmal or permanent high-grade AV block in the absence of AF</li> <li>- paroxysmal or permanent high-grade AV block in the presence of paroxysmal AF</li> <li>- paroxysmal or permanent high-grade AV block in the presence of persistent AF when attempts at restoring sinus rhythm are still planned.</li> </ul> <p>The device is designed to be used only in the right ventricle.</p>

Product name (sponsor)	ARTG summary	Functional description	Intended purpose
Micra AV2 MC2AVR1 Intracardiac pacemaker (Medtronic Australasia Pty Ltd)	<b>ARTG ID:</b> 455510 <b>Start date:</b> 17/07/2024 <b>Category:</b> Medical Device Class III <b>GMDN:</b> 60789 Intracardiac pacemaker	MR Conditional dual-chamber, transcatheter pacing system with SureScan technology is a programmable cardiac device that monitors and regulates the patient's heart rate by providing rate-responsive bradycardia pacing to the right ventricle and AV synchrony based on the mechanical sensing of atrial activity. It senses both the electrical activity and the mechanical activity of the patient's heart using sensing and pacing electrodes and an accelerometer enclosed in a miniature titanium capsule.	Micra AV2 Model MC2AVR1 is indicated for VDD pacing in patients when a dual-chamber transvenous pacing system is considered a poor option or not deemed necessary for effective therapy, and when a right ventricular transcatheter pacing system promoting AV synchrony at rest is acceptable. Conditions when a patient is considered a poor candidate for transvenous pacing may include, but are not limited to, tortuous anatomy, a need to preserve venous access, or increased risk of infection. The device provides AV synchrony at rest and rate-responsive (VVIR) pacing during periods of high patient activity. Device-mediated AV synchrony can vary depending on patient condition and activity levels, and it can be limited at high sinus rates. During periods of intermittent AV synchrony, the device will provide ventricular pacing support with an increased potential for pacing rate variability. Micra AV2 is indicated for use in patients who have experienced one of the following: <ul style="list-style-type: none"> <li>- paroxysmal or permanent high-grade AV block in the absence of AF</li> <li>- paroxysmal or permanent high-grade AV block in the presence of paroxysmal AF</li> <li>- paroxysmal or permanent high-grade AV block in the presence of persistent AF when attempts at restoring sinus rhythm are still planned.</li> </ul> The device is designed to be used only in the right ventricle.
Micra Introducer Model MI2355A Cardiovascular device introducer, non-steerable (Medtronic Australasia Pty Ltd)	<b>ARTG ID:</b> 221570 <b>Start date:</b> 24/03/2014 <b>Category:</b> Medical Device Class III <b>GMDN:</b> 57941 Cardiovascular device introducer, non-steerable	The Micra introducer is a single-use, disposable, hydrophilically coated sheath that provides a flexible and haemostatic conduit for the insertion of intravascular devices into the venous system to minimise blood loss. The system is comprised of 2 components: a dilator that accommodates a guidewire and an introducer.	The Micra introducer is intended to provide a conduit for the insertion of devices into the venous system and to minimise blood loss associated with such insertions.

#### Abbreviations

**AF** = atrial fibrillation, **ARTG** = Australian Register of Therapeutic Goods, **AV** = atrioventricular, **MR** = magnetic resonance.

#### Source

ARTG Public Summary documents. Verified by assessment group on 13 November 2024.



The Micra AV2 was listed on the ARTG in July 2024. It has a projected median longevity of 15.6 years (44% longer than the Micra AV). It also features improved automatic AV synchrony at heart rates between 80 and 100 beats per minute (and an upper tracking limit of 135 beats per minute), more customisable settings that reduce the need for manual programming by 50% and a lower tip pressure from the catheter delivery system during implantation.<sup>3</sup> The current MSAC application pertains to the Micra AV device, since the Micra AV2 was not included in the ARTG at the time of writing.

The applicant specified some prerequisites for Micra AV use, including a proficiency in femoral venous access and large-bore catheter manipulation, as well as the completion of a dedicated training course (online modules and in-person, provided free of charge). Support by a Medtronic Micra technical expert is recommended for at least the first 10 implants.

The Aveir VR LPM (Abbott Medical Australia Pty Ltd) was listed on the ARTG on 10 October 2024 (ARTG ID: 464035), along with a retrieval catheter (ARTG ID: 464038) and a programming interface unit (ARTG ID: 464039). In June 2023, United States Food and Drug Administration (U.S. FDA) approved a dual-chamber LPM, the Aveir™ DR Leadless System, developed by Abbott.<sup>4</sup> The system consists of 2 percutaneously implanted devices: the single-chamber AVEIR VR leadless pacemaker implanted in the right ventricle and the AVEIR AR single-chamber pacemaker implanted in the right atrium. No dual-chamber LPMs are currently available in Australia.

## 6. Proposal for public funding

This application is primarily to request listing of the Micra AV on the Prescribed List of Medical Devices and Human Tissue Products (PL) via the Tier 3 full health technology assessment (HTA) pathway, following MSAC consideration.

The proposed population is a subset of the population defined in the ARTG intended purpose for the Micra AV devices (see Table 1) and includes patients indicated for permanent pacing to treat bradycardia due to paroxysmal or permanent high-grade AV block who are in sinus rhythm. The following criteria also apply:

- A dual-chamber transvenous pacemaker (DC-TVPM) is considered a poor option (e.g. tortuous anatomy, a need to preserve venous access, increased risk of infection) or not deemed necessary for effective therapy.
- A right ventricular transcatheter pacing system promoting AV synchrony at rest is acceptable (i.e. atrial pacing or close to 100% AV synchronicity is not required).

The Micra AV is a permanent single-chamber implantable transcatheter LPM that is inserted via the femoral vein and implanted directly into the right ventricular myocardium, negating the need for transvenous wires. The device monitors the electrical and mechanical activity of the patient's heart (atrium and ventricle) and provides rate-responsive AV synchronous pacing to the right ventricle in response to bradycardia. Mechanical activity in the atrium is sensed by an internal 3-axis accelerometer. Similar to transvenous pacemakers, the Micra VR TPS has traditional remote monitoring capabilities (via a physical monitor), although it is not capable of Bluetooth® monitoring (via a mobile app) due to its small size (25.9 mm long and 6.7 mm diameter). A

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<sup>3</sup> Medtronic (2024). *Micra™ leadless pacemakers*, accessed 13 November 2024, <https://www.medtronic.com/content/dam/medtronic-wide/public/canada/products/cardiac-vascular/cardiac-rhythm/pacing-systems/micra-vr2-av2-portfolio-brochure.pdf>.

<sup>4</sup> U.S. Food and Drug Administration (2023). *Premarket approval*, accessed 13 November 2024, <https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P150035S003>.

generic Medtronic cardiac device programmer (provided free of charge) is used to program the device.<sup>5</sup> The Micra AV is not intended to be removed at the end of its service life but remains in situ, and either a new LPM is inserted in the right ventricle or an alternative pacing approach is used.

This application is also requesting a new Medicare Benefits Schedule (MBS) item for the insertion of a single-chamber leadless pacemaker (LPM) with atrioventricular (AV) synchronous pacing (Micra™ AV) for patients with bradycardia due to AV block who are in sinus rhythm.

The following existing MBS items can be used to claim for services associated with the Micra AV device:

- MBS item 38373, for percutaneous retrieval and replacement of a single-chamber ventricular LPM.
- MBS item 38374 for percutaneous retrieval of a single-chamber ventricular LPM.
- MBS item 38375 for removal of a single-chamber ventricular LPM by open surgical approach.

The applicant proposed an additional MBS item for percutaneous insertion of the Micra AV device at the same fee as for MBS item 38372 (percutaneous insertion of a single-chamber ventricular LPM) (see Table 2). The explanatory note for the item specifically indicates the patients for whom the device is not recommended, in accordance with the Micra AV device manual and examples stipulated by the PICO Advisory Sub-committee (PASC). However, it should be noted that MBS item 38372, as it is currently worded, can still be used for insertion of an LPM with AV pacing in patients: 'Leadless permanent cardiac pacemaker, single-chamber ventricular, percutaneous insertion of, for the treatment of bradycardia, including cardiac electrophysiological services'. Therefore, to avoid leakage, MBS item 38372 will need to be amended to limit its use to patients indicated for a LPM with ventricular pacing only.

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<sup>5</sup> Medtronic, Inc. (2020). *Medtronic Micra™ AV MC1AVR1*, accessed 13 November 2024, [https://wwwp.medtronic.com/crs-upload/letters/401/401\\_Micra\\_AV\\_Implant\\_Manual\\_with\\_Medical\\_Procedure\\_and\\_EMI\\_Precautions.pdf](https://wwwp.medtronic.com/crs-upload/letters/401/401_Micra_AV_Implant_Manual_with_Medical_Procedure_and_EMI_Precautions.pdf).

**Table 2 Proposed MBS items *with ESC proposed amendments***

<p><b>Category 3 – THERAPEUTIC PROCEDURES</b></p> <p><b>Group T8 – Surgical Operations</b></p> <p><b>Subgroup 6 – Cardio-Thoracic</b></p> <p><b>Subheading 4 – Miscellaneous Cardiac Procedures</b></p>
<p><b>MBS item *XXXX</b></p> <p>Leadless permanent cardiac pacemaker with atrioventricular synchronous pacing, single-chamber ventricular, percutaneous insertion of, for the treatment of bradycardia <del>due to atrioventricular block and who are in sinus rhythm, including cardiac electrophysiological services (by a cardiologist or cardiothoracic surgeon,</del></p> <p><i>a) For a patient:</i></p> <ol style="list-style-type: none"> <li><i>where a right ventricular transcatheter pacing system promoting AV synchrony at rest is acceptable; and</i></li> <li><i>with Paroxysmal or permanent high-grade AV block and</i></li> <li><i>in sinus rhythm; and</i></li> <li><i>where a DC-TVPM is contraindicated; and</i></li> </ol> <p><i>b) including cardiac electrophysiological services</i></p> <p>other than a service associated with a service to which item 38350 <i>or 38372</i> applies) (H)</p> <p>Multiple Operation Rule (Anaes.)</p>
<p>\$859.35 Benefit: 75% = \$644.55</p>
<p>(See para. TN.X.XX of explanatory notes to this Category)</p> <p>TN.X.XX</p> <p><b>Eligibility requirements for item XXXX</b></p> <p>The decision to implant a leadless permanent cardiac pacemaker with atrioventricular synchronous pacing should consider the benefits of transcatheter pacing versus the patient's need for continuous AV synchrony. <i>This item is intended (but not limited to) patients where TVPM is contraindicated, as follows:</i></p> <ul style="list-style-type: none"> <li><i>inaccessible or tortuous upper extremity venous system</i></li> <li><i>increased risk of infection</i></li> <li><i>history of venous thrombosis</i></li> </ul> <p>This item is not intended for use in patients who will not benefit from the AV synchronous mode (VDD), including:</p> <ul style="list-style-type: none"> <li>Sinus node dysfunction</li> <li>High sinus rates requiring atrial tracking</li> <li>Weak atrial contraction</li> <li>Frequent premature atrial or ventricular contractions where atrial tracking is required immediately after the premature beat</li> </ul>

Introduction of the Micra AV is not likely to affect the patient workup for pacing treatment. Patients with symptomatic bradycardia may first seek treatment from a hospital or general practitioner before being referred to a specialist cardiologist. The patient's history and physical examination and resting electrocardiogram (ECG) results are all important components of the medical evaluation to assess eligibility for a single-chamber LPM.<sup>6</sup> Further non-invasive assessments may include an exercise or ambulatory ECG, imaging, laboratory tests, genetic tests and sleep apnoea tests. When non-invasive examinations are not diagnostic, invasive testing (e.g. implantable cardiac monitors and electrophysiology studies) may be required.<sup>6</sup>

LPM insertion is performed as an inpatient service, either in the public or private hospital setting by specialist cardiologists (interventional cardiologist, cardiac electrophysiologist) or cardiac

<sup>6</sup> Kusumoto FM, et al. (2019). 2018 ACC/AHA/HRS guideline on the evaluation and management of patients with bradycardia and cardiac conduction delay. A report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation* 140(8):e382-e482.

surgeons in a cardiac catheterisation laboratory or operating room. The procedure is usually performed under local anaesthetic.<sup>7</sup> The healthcare resources required to implant a DC-TVPM (the nominated comparator), including anaesthesia, the professional service itself and hospitalisation are similar to those required to deliver the Micra AV device. The frequency of patient monitoring and duration of stay are the same for both procedures, with patients generally being admitted overnight. According to Palmisano et al. (2021)<sup>8</sup> and an Australian study by Denman et al. (2019)<sup>7</sup>, the length of time required to insert an LPM, once proficiency is achieved, is similar to that for a DC-TVPM (around 30 minutes).

No key issues with the proposed descriptors have been identified. The 2021 European Society of Cardiology (ESC)<sup>9</sup> guidelines state that LPMs should be considered as an alternative to transvenous pacemakers when no upper extremity venous access exists or when risk of device pocket infection is particularly high, such as in patients with a previous infection or those on haemodialysis; and LPMs may be considered as an alternative to standard single-lead ventricular pacing, taking into consideration life expectancy and using shared decision-making. Guidelines from the American College of Cardiology (ACC), American Heart Association (AHA) and Heart Rhythm Society (HRS)<sup>6</sup> noted that identifying patient populations that will benefit the most from LPMs will require further investigation, and that the potential interaction of LPMs with other cardiac devices is still unclear.

## 7. Population

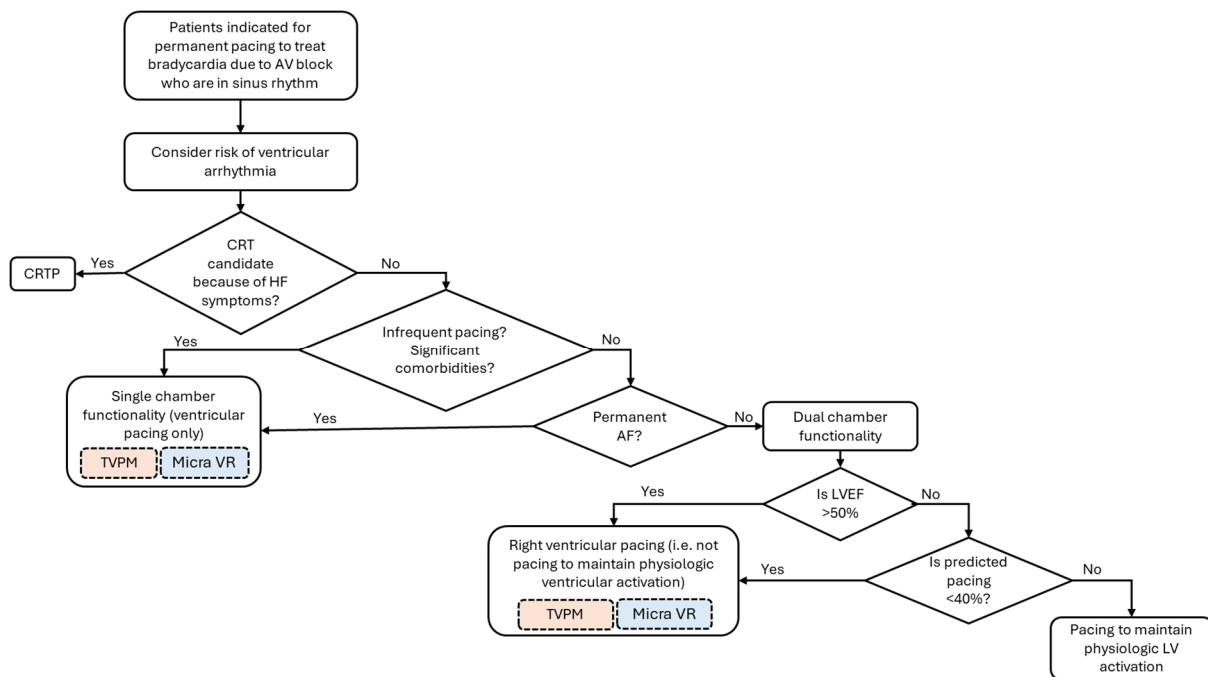
One population, intervention, comparator and outcome (PICO) set was defined for the proposed technology, the Micra AV LPM, as an alternative to standard DC-TVPMs in select patients (see Table 3). The current clinical management algorithm for patients indicated for permanent pacing to treat bradycardia due to AVB who are in sinus rhythm in the absence of the Micra AV device is shown below in Figure 1. Micra AV would also replace the Micra VR as an option for right ventricular pacing in patients indicated for a pacemaker with dual-chamber functionality. The clinical management algorithm incorporating the Micra AV device was based on the 2018 guidelines developed by the ACC, AHA and HRS<sup>6</sup>, as well as consultation with several Australian cardiologists.

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<sup>7</sup> Denman RA, et al. (2019). Leadless permanent pacing: A single centre Australian experience. *Heart Lung Circ* 28(11):1677-1682.

<sup>8</sup> Palmisano P, et al. (2021). Leadless pacemaker versus transvenous single-chamber pacemaker therapy: peri-procedural aspects, utilization of medical resources and patient acceptance. *Expert Rev Med Devices* 18(5):483-491.

<sup>9</sup> Glikson M, et al. (2021), 2021 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy. *Eur Heart J* 42(35):3427-3520.



**Figure 1 Current clinical management algorithm**

Abbreviations: AF, atrial fibrillation; AV, atrio-ventricular; CRT, cardiac resynchronisation therapy; CRTP, cardiac resynchronisation therapy pacemaker; HF, heart failure; LV, left ventricular; LVEF, left ventricular ejection fraction; TVPM, transvenous pacemaker. Source: 1772 Applicant Derived Assessment Report (ADAR)

The Micra AV LPM is indicated for patients who require permanent pacing to treat bradycardia due to paroxysmal or permanent high-grade AV block and who are in sinus rhythm. The following criteria also apply:

- A dual-chamber transvenous pacing system is considered a poor option (e.g. tortuous anatomy, a need to preserve venous access, increased risk of infection) or not deemed necessary for effective therapy.
- A right ventricular transcatheter pacing system promoting AV synchrony at rest is acceptable (i.e. atrial pacing or close to 100% AV synchronicity is not required).

Given that the Micra AV device senses atrial activity, it is not indicated for patients with atrial fibrillation (AF) or those who require pacing to the atrium (i.e. patients with sinus bradycardia with or without chronotropic incompetence) or close to 100% AV synchronicity. The applicant noted that these criteria require a degree of subjective interpretation by the clinician in terms of determining patient need for the device. However, it is unclear how this is determined or what the cutoff is in terms of the lower or upper limit of AV synchronicity permissible in the proposed MBS population.

Per the first bullet point in the criteria listed above, there are 2 potential subpopulations in the MBS proposed population of patients with bradycardia due to paroxysmal or permanent high-grade AV block who are in sinus rhythm: a) those for whom a dual-chamber transvenous pacing system is not an option because of, for example, tortuous anatomy, a need to preserve venous access or increased risk of infection; and b) those for whom a dual-chamber transvenous pacing system is an option but is not necessary for effective therapy. This difference affects the choice of comparator since the appropriate comparator for the former population is an epicardial pacemaker or no pacing, whereas the appropriate comparator for the latter population is a DC-TVPM. There is also a third small group noted in the PICO Confirmation: people who currently

have a Micra VR implant who might benefit from switching to the Micra AV. The commentary's clinical expert confirmed that this would only occur in the rare instance that a lack of AV synchrony caused problematic symptoms. Notwithstanding the applicant's decision to exclude Micra VR as a clinical comparator, ESC noted that this meant that no evidence was presented to support the higher proposed PL benefit for Micra AV.

**Table 3 PICO criteria for assessing single-chamber leadless pacing with atrioventricular synchronous pacing in patients with bradycardia and who are in sinus rhythm**

Component	Description
Population	<p>Patients who are indicated for permanent pacing to treat bradycardia due to paroxysmal or permanent high-grade AV block and who are in sinus rhythm.</p> <p>The following criteria also apply:</p> <ul style="list-style-type: none"> <li>• A dual-chamber transvenous pacing system is considered a poor option (e.g. tortuous anatomy, a need to preserve venous access, increased risk of infection) or not deemed necessary for effective therapy.</li> <li>• A right ventricular transcatheter pacing system promoting AV synchrony at rest is acceptable (i.e. atrial pacing or close to 100% AV synchronicity is not required).</li> </ul>
Intervention	Insertion of a LPM into the right ventricle, that promotes AV synchronous pacing (Medtronic Micra AV)
Comparator	<p>Primary: insertion of a conventional DC-TVPM</p> <p>Secondary: insertion of a Micra VR LPM (if applicant intends to seek a higher PL benefit for the Micra AV) <sup>a</sup></p>
Outcomes <sup>bb</sup>	<p><b>Technical performance</b></p> <p>Pacing performance (sensing, impedance, pacing threshold, AV synchronicity, rate-responsiveness)</p> <p>Battery life</p> <p><b>Patient-relevant effectiveness</b></p> <p>Mortality (all-cause, cardiovascular)</p> <p>Exercise capacity</p> <p>Switch to an alternative device (a different pacemaker or defibrillator)</p> <p>Health-related quality of life</p> <p>Patient satisfaction</p> <p>Any differential outcome by patient characteristics (e.g. age, comorbidities, pacing indications)</p> <p><b>Safety</b></p> <p>Implant success/failure rates</p> <p>Procedure-related mortality and major complications (acute, chronic)</p> <p>Major device-related complications (device dislodgement, device malfunction, battery failure, device infection, pacemaker-induced arrhythmia)</p> <p>Pacemaker syndrome</p> <p>Device revision, retrieval, replacement, explantation, reintervention rates</p> <p>Any serious adverse events</p> <p><b>Healthcare resources</b></p> <p>Cost of the device and consumables</p> <p>Procedure-related costs</p> <p>Follow-up evaluation and monitoring costs</p> <p>Costs associated with the management of complications</p> <p><b>Cost-effectiveness</b></p> <p><b>Total Australian Government health care costs (e.g. public/private hospital, PHI, OOP)</b></p>
<p>Systematic review questions:</p> <p>What is the safety, effectiveness and cost-effectiveness of single-chamber leadless pacing with atrioventricular synchronous pacing compared to a dual-chamber transvenous pacemaker in patients with bradycardia due to paroxysmal or permanent high-grade atrioventricular block and who are in sinus rhythm and are ineligible for or do not require a DC-TVPM?</p>	

#### **Abbreviations**

**AV** = atrioventricular, **DC-TVPM** = dual-chamber transvenous pacemaker, **LPM** = leadless pacemaker, **OOP** = patient out-of-pocket, **PHI** = private health insurer, **PL** = Prescribed List of Medical Devices and Human Tissue Products.

#### **Notes**

**a** = The applicant claimed that this secondary comparator is unnecessary because it is clinically inappropriate to use the Micra VR in the proposed patient population when the Micra AV is available. Also, a formal comparison between the Micra VR and AV is not necessary for the very small group of patients who currently have a Micra VR implant but might benefit from switching to the Micra AV. This reasoning was confirmed by the assessment group's clinical expert.

**b** = The following outcomes were not addressed in the submission because no evidence was available in the included studies: cardiovascular or procedure-related mortality, exercise capacity, patient satisfaction, implant success and failure rates and differential outcome by patient characteristics. Quality of life, battery life and AV synchronicity were addressed with supportive evidence only.

The proposed population is a subgroup of the overall patient population that would be eligible for a DC-TVPM. Based on the usage statistics for MBS item 38356 (insertion, removal or replacement of dual-chamber permanent transvenous electrodes), the applicant reasonably estimated that approximately 8,900 to 9,700 implantation procedures will be performed for DC-TVPM each year from 2024 to 2027. Of those, it was estimated that up to 35% will be in patients with AV block and normal sinus rhythm, equating to approximately 3,100 to 3,400 patients each year. However, some of the services provided under MBS item 38356 relate to removal and replacement of existing leads, so the annual number of patients is likely to be lower than the estimate because lead complications do not occur with Micra AV. In addition, the estimate does not include the patients without AF in which the Micra AV will supplant use of the Micra VR and those who currently have a Micra VR implant but might benefit from switching to the Micra AV. It is unclear how these additional patients will affect the proposed population size. The applicant noted advice from Australian clinical experts that not more than 5% of patients in sinus rhythm with AV block would be contraindicated for a transvenous option or have a very high clinical need for an LPM.

The current MSAC application pertains to the Micra AV device, since the Micra AV2 was not included in the ARTG at the time of writing. However, the Micra AV2 features improved automatic AV synchrony at heart rates between 80 and 100 beats per minute (and an upper tracking limit of 135 beats per minute), which could possibly expand the population to slightly 'younger' individuals.<sup>3</sup>

The applicant-developed assessment report (ADAR) largely addresses the requirements of the confirmed PICO, although some of the prespecified outcomes were not reported in the included studies (Table 3). In addition, it would have been helpful to specify a maximum proportion of patients allowed with concomitant procedures in the included studies to minimise confounding (<10% would have been appropriate) and clear application of the selection criteria.

## **8. Comparator**

The nominated primary comparator is insertion of a conventional DC-TVPM, which is appropriate for patients with bradycardia due to paroxysmal or permanent high-grade AV block who are in sinus rhythm. However, it should be noted that for the subgroup of these patients who are ineligible to receive a DC-TVPM (e.g. because of tortuous anatomy, a need to preserve venous access or increased risk of infection), the appropriate comparator would be an epicardial pacemaker or no pacing. In the small group of patients who currently have a Micra VR implant but might benefit from switching to the Micra AV (noted in the PICO Confirmation), the appropriate comparator would be the Micra AV. However, the assessment group's clinical expert stated that this would only be considered in the rare instance that a lack of AV synchrony caused problematic symptoms.

A DC-TVPM consists of a pulse generator (containing the battery and the machinery for sensing and timing of electrical impulses) and 2 leads (insulated wires that deliver electrical impulses from the pulse generator to the heart). The pulse generator is implanted in a subcutaneous pocket created in the anterior chest wall. Two leads are inserted percutaneously either via subclavian, cephalic or axillary veins and guided transvenously past the tricuspid valve into the ventricle and atrium using fluoroscopy. The leads are attached to the myocardium either with a screw or tines, which become fixed via granulation tissue formation. When the DC-TVPM is used in DDD mode, both the ventricle and atrium are sensed and paced.

DC-TVPMs associated procedures are currently funded through the MBS items outlined in Table 4.



**Table 4 MBS items associated with a DC-TVPM and leads**

Item no.	Description	Fee and benefit
38353	PERMANENT CARDIAC PACEMAKER, insertion, removal or replacement of, not for cardiac resynchronisation therapy, including cardiac electrophysiological services where used for pacemaker implantation Multiple Operation Rule (Anaes.) (See para. TN.8.60 of explanatory notes to this Category) <sup>a</sup>	Fee: \$291.00 Benefit: 75% = \$218.25
38356	DUAL-CHAMBER PERMANENT TRANSVENOUS ELECTRODES, insertion, removal or replacement of, including cardiac electrophysiological services where used for pacemaker implantation Multiple Operation Rule (Anaes.) (See para. TN.8.60 of explanatory notes to this Category) <sup>a</sup>	Fee: \$953.90 Benefit: 75% = \$715.45
38358	Extraction of one or more chronically implanted transvenous pacing or defibrillator leads, by percutaneous method, with locking stylets and snares, with extraction sheaths (if any), if: (a) the leads have been in place for more than 6 months and require removal; and (b) the service is performed: (i) in association with a service to which item 61109 or 60509 applies; and (ii) by a specialist or consultant physician who has undertaken the training to perform the service; and (iii) in a facility where cardiothoracic surgery is available and a thoracotomy can be performed immediately and without transfer; and (c) if the service is performed by an interventional cardiologist—a cardiothoracic surgeon is in attendance during the service (H) Multiple Operation Rule (Anaes.) (Assist) (See para. TN.8.64, TN.8.214 of explanatory notes to this Category) <sup>b,c</sup>	Fee: \$3,267.35 Benefit: 75% = \$2,450.55

**Abbreviations**

no. = number, DC-TVPM = dual-chamber transvenous pacemaker.

**Notes**

**a** = TN.8.60: The fees for the insertion of a pacemaker (Items 38350, 38353 and 38356) cover the testing of cardiac conduction or conduction threshold, etc. related to the pacemaker and pacemaker function. Accordingly, additional benefits are not payable for such routine testing under Item 38209 or 38212 (Cardiac electrophysiological studies).

**b** = TN.8.64: For the purposes of item 38358, specialists or consultant physicians claiming this item must have training recognised by the Lead Extraction Advisory Committee of the Cardiac Society of Australia and New Zealand, and the Department of Human Services notified of that recognition. The procedure should only be undertaken in a hospital capable of providing cardiac surgery.

**c** = TN.8.214: International guidelines and claiming guide for extraction of leads: International guidelines state that delays from injury to open access to the heart of more than 5 to 10 minutes are often associated with a fatal outcome. Preparations for this procedure should provide for this rare but life-threatening circumstance. Claiming guide: When the service to which item 38358 applies is provided to a patient by an accredited interventional cardiologist, the following claiming will apply:

- Item 38358 is to be claimed by the accredited interventional cardiologist; and
- Item 90300 is to be claimed by the standby cardiothoracic surgeon.

When the service to which item 38358 applies is provided to a patient by an accredited cardiothoracic surgeon, the following claiming will apply:

- Item 38358 is to be claimed by the accredited cardiothoracic surgeon only.

**Source**

MBS online. Verified by assessment group on 13 November 2024.

The PICO Confirmation specified insertion of a Micra VR LPM as a secondary comparator if the applicant intended to seek a higher PL benefit for the Micra AV. The proposed benefit for the Micra AV device in this ADAR is \$redacted, which is higher than that for the Micra VR device (\$10,083). ESC noted that the applicant argued that given the small overlap in the populations

between the 2 devices ( $\leq 5\%$ ), and the fact that this overlap was due to VR being the only LPM available at the time, a formal comparison with Micra VR was not provided. The applicant consulted 3 Australian cardiologists who confirmed that: a) it would be clinically inappropriate to use the Micra VR in the proposed patient population when the Micra AV is available; and b) a formal comparison between the Micra VR and AV is not necessary for the very small group of patients who currently have a Micra VR implant but might benefit from switching to the Micra AV.

MSAC noted that no information comparing the design, characteristics, or specifications of the Micra AV and Micra VR were provided in the ADAR, but that this information may be required for any subsequent PL application for the Micra AV.

## **9. Summary of public consultation input**

Consultation input was received from one medical, health, or other (non-consumer) organisation and one consumer organisation.

The organisations that submitted input were:

- Hearts4Heart
- Abbott Medical Australia Pty Ltd (Abbott)

### **Level of support for public funding**

Both organisations supported public funding of a wider range of clinically safe, effective, and cost-effective leadless technology options for indicated patients in Australia. However, Abbott referred to inconsistencies in the application relating to the PICO, as described below.

### **Comments on PICO**

Abbott, developers of a competitor dual chamber leadless pacemaker system, considered that a single chamber pacemaker would be the most appropriate comparator for the Micra AV, based on the proposed population and technical features of the proposed technology. as it is proposed for a population in need of single chamber pacing and sensing of the atrium (as opposed to both chambers of the heart). Abbott provided input regarding its consideration of the appropriate category and product subgroup for the PL if approved for listing.

### **Perceived Advantages**

Advantages of the technology were noted by Hearts4Heart, including:

- Small size and improved battery life.
- Minimally invasive procedure, leading to fewer post-implant activity restrictions and no obstructions to shoulder movement.
- Improved quality of life due to leadless technology, including ability to participate in work, physical activity, and community life.
- Increased safety of leadless pacing compared to conventional single-chamber pacing, including psychiatric patients, kidney failure patients, patients with disabilities, and the young and active population.
- Reduced risk of infection due to lead infections, resulting in the reduced need for long hospital stays and antibiotic use.
- No visible sign of a medical device under skin and absence of a scar post-implantation.

## 10. Characteristics of the evidence base

A predefined post hoc subgroup analysis of the Micra AV coverage with evidence development (CED) study formed the main evidence for this submission (Table 5).

**Table 5 Key features of the included evidence comparing the Micra AV LPM with DC-TVPMs**

Reference	N	Design/duration	Risk of bias	Patient population	Outcome(s)	Use in modelled evaluation
Micra AV CED NCT04235491	41,979 <sup>a</sup>	Non-randomised comparative study, prospective (treatment arm)/retrospective (control arm) 5 February 2020 to 31 December 2021	Low <sup>b</sup>	United States Medicare fee-for-service beneficiaries implanted with a Micra AV or DC-TVPM Patients identified using the ICD-10-Procedure Coding System and the Current Procedural Terminology codes	<b>Primary:</b> Acute complication rate (30 days) and 2-year survival <b>Secondary:</b> Chronic complication and device-related reintervention rates at 2 years	Yes <sup>c</sup>

### Abbreviations

**CED** = coverage with evidence development, **DC-TVPM** = dual-chamber transvenous pacemaker, **ICD** = International Classification of Disease.

### Notes

**a** = Subgroup of patients with atrioventricular block without atrial fibrillation, derived from the main study (N=118,110); the post hoc subgroup analysis was defined a priori

**b** = Assessed with the National Heart, Lung and Blood Institute (NHLBI) Study Quality Assessment tool for observational and cross-sectional studies

**c** = Adjusted rates used for economic model

### Source

Full CED study: Crossley (2024)<sup>10</sup>, El-Chami (2024)<sup>11</sup>

Since the Micra AV CED study did not capture data on quality of life (QoL), AV synchrony or battery life, 5 additional studies were included as supportive evidence: 2 single-arm studies and 1 modelling study on the Micra AV or AV2 for data on battery life and AV synchronicity;<sup>12</sup> and 2 prospective non-randomised studies comparing Micra VR with conventional pacemakers with respect to QoL (Table 6).<sup>8 13</sup> These 5 studies did not undergo quality appraisal.

<sup>10</sup> Crossley GH, et al. (2024). Outcomes of patients implanted with an atrio-ventricular synchronous leadless ventricular pacemaker in the Medicare population. *Heart Rhythm* 2024;21(1):66-73.

<sup>11</sup> El-Chami M, et al. (2024). Two-year outcomes of Micra AV leadless pacemakers in the Micra AV CED study. *Europace* 26(11):euae273.

<sup>12</sup> Chinitz LA, et al. (2023). Ambulatory atrioventricular synchronous pacing over time using a leadless ventricular pacemaker: primary results from the AccelAV study. *Heart Rhythm* 20(1):46-54; Garweg, C., et al. (2024). A leadless ventricular pacemaker providing atrioventricular synchronous pacing in the real-world setting: 12-month results from the Micra AV post-approval registry. *Heart Rhythm* 21(10):1939-1947; Leal M, et al. (2024). Device longevity and AV synchrony algorithm modeling of a leadless pacemaker 1 family: a virtual patient analysis.

<sup>13</sup> Cabanas-Grandío P, et al. (2020). Quality of life of patients undergoing conventional vs leadless pacemaker implantation: a multicenter observational study. *J Cardiovasc Electrophysiol* 31(1):330-336.

**Table 6 Key features of supportive evidence to inform QoL, AV synchrony and battery life for the Micra AV LPM**

Reference	Design/duration	Patient population	Outcome(s)	Use in modelled evaluation
Cabanas-Grandío 2020	Multicentre, observational study at 4 tertiary hospitals in Spain December 2016 to March 2018	Patients aged $\geq 18$ years with an indication for single-chamber pacemaker implantation Conventional PM (N=64) Micra VR (N=42)	QoL (SF-36)	No
Palmisano 2021	Prospective, single-centre PSM cohort study at a single centre in Italy February 2016 to May 2020	Patients who met class I or II guideline recommendations for de novo ventricular pacing with a single-chamber PM Conventional PM (N=77) Micra VR (N=77)	QoL (SF-36)	Yes
AccelAV (Chinitz 2023)	Prospective, multicentre, single-arm study at 20 centres in the USA and Hong Kong June 2020 to September 2021	Patients age $\geq 18$ years who planned to undergo Micra AV implantation for an approved indication Micra AV (N=152)	AVS QoL (EQ-5D-3L)	Yes (utility data)
Micra AV PAR (Garweg 2024)	Prospective, single-arm, observational registry data from 97 centres in 19 countries February 2020 and April 2022	All patients intended to be implanted with a market approved Micra AV device at participating centres Micra AV (N=801)	AVS Battery longevity Incidence of pacemaker syndrome	No
Leal 2024	Modelling and simulation-based analyses based on real-world pacing and accelerometer data from the AccelAV study were used to create virtual patients and compare AVS between enhanced and original algorithms to estimate the AVS rate of the Micra AV2 and Micra VR2	Micra AV2 analysis: pacing and accelerometer parameters from a deidentified CareLink analysis of 999 Micra AV devices that had been implanted for longer than 6 months	AVS Battery longevity	Yes (model duration)

**Abbreviations**

AVS = atrioventricular synchronicity, PM = pacemaker, PSM = propensity score matched, QoL = quality of life.

**Methodological considerations****Study selection and data extraction**

The selection of databases searched was adequate, and the search strategies were broad enough to capture any relevant published literature. However, relevant conference proceedings and other grey literature sources (including the INAHTA HTA database) were not searched, which is a limitation given that there were likely to be few published studies. However, this was partially offset by the searches conducted in the applicant's trials database and hand searching the reference lists of retrieved studies.

The listed study selection criteria appear to have been uniformly and correctly applied. However, there were very few details reported about how the study selection and data extraction processes were undertaken. This may, in part, be because the main evidence for this submission was a post

hoc analysis of data from the applicant's device registry. However, best practice for systematic reviews requires that data extraction forms and procedures be established a priori, regardless of the reviewers' expectations of what the final evidence base will include. Single-arm studies were not included for safety outcomes, which is appropriate given the size of the Micra CED study. Also, since the Micra AV has only been widely available in Europe and the USA since 2020, it is unlikely that expanding the study eligibility would provide any useful information on longer-term safety outcomes (i.e. beyond 2 years).

### **Synthesis of evidence**

The quality of the Micra CED study was assessed with the National Heart, Lung and Blood Institute (NHLBI) Study Quality Assessment tool for observational and cross-sectional studies, although no details were provided about how the quality appraisal process was conducted. The Micra CED study was deemed to be of good quality, despite significant differences in several baseline patient characteristics and prognostic factors between the LPM and DC-TVPM treatment groups, because it used a propensity score weighting method to create a comparison of patients at clinical equipoise with respect to the treatments being compared. The weighting method adjusted for 31 baseline and encounter characteristics. Outcomes were also adjusted for age, sex and comorbid conditions. However, it should be noted that the propensity score weighting method is not necessarily exhaustive, since it cannot adjust for patient characteristics that are not measured but may influence a clinician's decision regarding treatment allocation. For example, it appears likely that the LPM group included patients who were ineligible to receive a DC-TVPM (23% of patients in the LPM group in the larger Micra CED study), which may lead to selection bias. These patients tend to have a higher all-cause mortality rate than those who are eligible for both devices,<sup>10</sup> and it is unclear how many of these patients were in the non-AF subgroup analysed in this submission. This is a significant confounding factor, given that the appropriate comparator for these patients is an epicardial pacemaker or no pacing at all, that is not necessarily offset by the propensity score matching method used to correct for the many other differences between the 2 treatment groups at baseline.

## **11. Comparative safety**

The safety outcomes discussed are those from the Micra AV CED study post hoc subgroup analysis.

### **Acute complications (30 days)**

Patients implanted with a Micra AV had a significantly lower incidence of acute complications within 30 days than those who received a DC-TVPM (8.7% versus 10.4%; relative risk [RR] 0.83, 95% confidence interval [CI] 0.75, 0.92) (Table 7). The main underlying complications in the LPM group were deep vein thrombosis, puncture site events and cardiac effusion and tamponade. In contrast, the acute complications for DC-TVPM were mostly driven by device-related complications such as device dislodgment and breakdown, haemorrhage, pain and pocket complications.

Without further data on the extent and severity of the device-related complications in the DC-TVPM group and how they were remedied, it is difficult to determine whether this represents a clinically important difference. A device-related complication that can be managed easily has a very different outcome to a complication that requires device removal. Since the Micra AV device is designed to remain in situ if it fails, it is unclear whether device dislodgment or other mechanical failure can escalate into a serious adverse event. The vascular events more

frequently associated with LPM implantation, including arteriovenous fistula and vascular aneurysm at the puncture site, embolism and thrombosis may not be immediately life-threatening and often require only conservative management, but their potential to become so should be considered. In addition, although adjusted rates of cardiac perforation are similar between the 2 devices, it has been noted that major complications related to cardiac perforation following implantation of the Micra VR, which is identical to the Micra AV in size and shape, tend to be more severe than for patients who receive a transvenous pacemaker.<sup>14</sup>

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<sup>14</sup> U.S. FDA (2021). *Leadless pacing systems: Risk of major complications related to cardiac perforation during implantation – Letter to health care providers*, accessed 13 November 2024, <https://www.fda.gov/media/154761/download>; Hauser RG, et al. (2022). Leadless pacemaker perforations: Clinical consequences and related device and user problems. *J Cardiovasc Electrophysiol* 2022 33(2):154-159.

**Table 7 Acute complications at 30 days in the Micra AV CED study (AV block without AF subgroup)**

	Unadjusted					Adjusted <sup>a</sup>				
Complication	Micra AV	DC-TVPM	RR [95% CI]	RD [95% CI]	P value	Micra AV	DC-TVPM	RR [95% CI]	RD [95% CI]	P value
N	3,902	38,077				3,902	38,077			
<b>Overall (any) complications, n (%)<sup>b</sup></b>	354 (9.1)	3561 (9.4)	0.97 [0.87, 1.08]	-0.00 [-0.01, 0.01]	0.6598	339 (8.7)	3978 (10.4)	0.83 [0.75, 0.92]	-0.02 [-0.03, -0.01]	<b>0.0009</b>
Embolism and thrombosis	175 (4.5)	1176 (3.1)	1.45 [1.24, 1.70]	0.01 [0.01, 0.02]	<b>&lt;0.0001</b>	167 (4.3)	1384 (3.6)	1.18 [1.01, 1.38]	0.01 [-0.00, 0.01]	<b>0.0492</b>
Deep vein thrombosis	120 (3.1)	775 (2.0)	1.51 [1.25, 1.83]	0.01 [0.00, 0.02]	<b>&lt;0.0001</b>	116 (3.0)	915 (2.4)	1.24 [1.02, 1.50]	0.01 [0.00, 0.01]	<b>0.0417</b>
Pulmonary embolism	64 (1.6)	490 (1.3)	1.27 [0.98, 1.65]	0.00 [-0.00, 0.01]	0.0624	60 (1.5)	577 (1.5)	1.01 [0.78, 1.32]	0.00 [-0.00, 0.00]	0.9174
Thrombosis due to cardiac device	*	24 (0.1)	–	–	<b>0.0473</b>	*	28 (0.1)	–	–	0.1495
Embolism due to cardiac device	*	*	–	–	0.5398	*	*	–	–	0.7402
Events at puncture site	33 (0.8)	92 (0.2)	3.50 [2.35, 5.20]	0.01 [0.00, 0.01]	<b>&lt;0.0001</b>	30 (0.8)	145 (0.4)	2.02 [1.36, 2.99]	0.00 [0.00, 0.01]	<b>0.0019</b>
Arteriovenous fistula	17 (0.4)	27 (0.1)	6.14 [3.35, 11.26]	0.00 [0.00, 0.01]	<b>&lt;0.0001</b>	14 (0.4)	73 (0.2)	1.87 [1.06, 3.31]	0.00 [-0.00, 0.00]	0.0966
Vascular aneurysm	19 (0.5)	66 (0.2)	2.81 [1.69, 4.67]	0.00 [0.00, 0.01]	<b>&lt;0.0001</b>	19 (0.5)	75 (0.2)	2.47 [1.50, 4.09]	0.00 [0.00, 0.01]	<b>0.0006</b>
Cardiac effusion/perforation	60 (1.5)	239 (0.6)	2.45 [1.85, 3.24]	0.01 [0.01, 0.01]	<b>&lt;0.0001</b>	61 (1.6)	277 (0.7)	2.15 [1.63, 2.83]	0.01 [0.00, 0.01]	<b>&lt;0.0001</b>
Cardiac perforation	8 (0.2)	34 (0.1)	2.30 [1.06, 4.96]	0.00 [-0.00, 0.00]	<b>0.0396</b>	8 (0.2)	40 (0.1)	1.95 [0.91, 4.17]	0.00 [-0.00, 0.00]	0.0793
Pericardial effusion	11 (0.3)	41 (0.1)	2.62 [1.35, 5.09]	0.00 [0.00, 0.00]	<b>0.0037</b>	12 (0.3)	48 (0.1)	2.44 [1.30, 4.59]	0.00 [0.00, 0.00]	<b>0.0120</b>
Cardiac tamponade	52 (1.3)	194 (0.5)	2.62 [1.93, 3.55]	0.01 [0.00, 0.01]	<b>&lt;0.0001</b>	53 (1.4)	223 (0.6)	2.32 [1.72, 3.12]	0.01 [0.00, 0.01]	<b>&lt;0.0001</b>
Device-related complication	62 (1.6)	1,480 (3.9)	0.41 [0.32, 0.53]	-0.02 [-0.03, -0.02]	<b>&lt;0.0001</b>	58 (1.5)	1552 (4.1)	0.36 [0.28, 0.47]	-0.03 [-0.03, -0.02]	<b>&lt;0.0001</b>
Mechanical	19 (0.5)	501 (1.3)	0.37 [0.23, 0.58]	-0.01 [-0.01, -0.01]	<b>&lt;0.0001</b>	20 (0.5)	515 (1.4)	0.38 [0.24, 0.59]	-0.01 [-0.01, -0.01]	<b>&lt;0.0001</b>

	Unadjusted					Adjusted <sup>a</sup>				
Complication	Micra AV	DC-TVPM	RR [95% CI]	RD [95% CI]	P value	Micra AV	DC-TVPM	RR [95% CI]	RD [95% CI]	P value
N	3,902	38,077				3,902	38,077			
breakdown of CIED				-0.01]					-0.01]	
Device dislodgment	16 (0.4)	795 (2.1)	0.20 [0.12, 0.32]	-0.02 [-0.02, -0.01]	<b>&lt;0.0001</b>	16 (0.4)	803 (2.1)	0.19 [0.12, 0.32]	-0.02 [-0.02, -0.01]	<b>&lt;0.0001</b>
Other mechanical complication of CIED	15 (0.4)	289 (0.8)	0.51 [0.30, 0.85]	-0.00 [-0.01, -0.00]	<b>0.0071</b>	14 (0.4)	277 (0.7)	0.49 [0.29, 0.84]	-0.00 [-0.01, -0.00]	<b>0.0076</b>
Infection due to device, implant, grafts	0 (0.0)	30 (0.1)	0.16 [0.01, 2.61]	-0.00 [-0.00, -0.00]	NE	0 (0.0)	31 (0.1)	0.15 [0.01, 2.53]	-0.00 [-0.00, -0.00]	NE
Haemorrhage due to device, implant, grafts	*	76 (0.2)	–	–	0.0586	*	88 (0.2)	–	–	0.0524
Pain due to device, implant, grafts	*	55 (0.1)	–	–	0.2883	*	71 (0.2)	–	–	0.1600
Stenosis due to device, implant, grafts	*	44 (0.1)	–	–	0.4766	*	46 (0.1)	–	–	0.6412
Pocket complications	N/A	241 (0.6)	–	–	NE	N/A	268 (0.7)	–	–	NE
Other complications	77 (2.0)	998 (2.6)	0.75 [0.60, 0.95]	-0.01 [-0.01, -0.00]	<b>0.0208</b>	72 (1.9)	1092 (2.9)	0.64 [0.51, 0.81]	-0.01 [-0.01, -0.01]	<b>0.0007</b>
AMI, device-related	*	23 (0.1)	–	–	0.8347	*	26 (0.1)	–	–	0.4704
Hematoma-post-procedural	13 (0.3)	81 (0.2)	1.57 [0.87, 2.81]	0.00 [-0.00, 0.00]	0.1722	12 (0.3)	99 (0.3)	1.18 [0.65, 2.15]	0.00 [-0.00, 0.00]	0.6450
Haemorrhage-post-procedural	13 (0.3)	60 (0.2)	2.11 [1.16, 3.85]	0.00 [-0.00, 0.00]	<b>0.0116</b>	13 (0.3)	69 (0.2)	1.84 [1.02, 3.32]	0.00 [-0.00, 0.00]	0.0666
Intraoperative cardiac arrest	15 (0.4)	100 (0.3)	1.46 [0.85, 2.52]	0.00 [-0.00, 0.00]	0.1811	15 (0.4)	128 (0.3)	1.14 [0.67, 1.95]	0.00 [-0.00, 0.00]	0.6634
Pericarditis	34 (0.9)	262 (0.7)	1.27 [0.89, 1.81]	0.00 [-0.00, 0.00]	0.2772	31 (0.8)	270 (0.7)	1.12 [0.77, 1.62]	0.00 [-0.00, 0.00]	0.5797



	Unadjusted					Adjusted <sup>a</sup>				
Complication	Micra AV	DC-TVPM	RR [95% CI]	RD [95% CI]	P value	Micra AV	DC-TVPM	RR [95% CI]	RD [95% CI]	P value
N	3,902	38,077				3,902	38,077			
									0.00]	
Vascular complication	18 (0.5)	74 (0.2)	2.37 [1.42, 3.97]	0.00 [0.00, 0.00]	<b>0.0011</b>	17 (0.4)	88 (0.2)	1.89 [1.12, 3.17]	0.00 [-0.00, 0.00]	<b>0.0204</b>
Hemothorax	*	*	–	–	0.4235	*	*	–	–	0.4791
Pneumothorax	N/A	495 (1.3)	–	–	NE	N/A	531 (1.4)	–	–	NE
<b>30-day mortality</b>	242 (6.2)	772 (2.0)	3.06 [2.66, 3.52]	0.04 [0.03, 0.05]	<b>&lt;0.0001</b>	226 (5.8)	1134 (3.0)	1.94 [1.69, 2.23]	1.94 [1.69, 2.23]	<b>&lt;0.0001</b>

#### **Abbreviations**

**AF** = atrial fibrillation, **AVB** = atrioventricular block, **AMI** = acute myocardial infarction, **CI** = confidence interval, **CIED** = cardiovascular implantable electronic device, **DC-TVPM** = dual-chamber transvenous pacemaker, **NA** = not applicable, **NE** = not estimable, **RD** = risk difference, **RR**, relative risk.

#### **Notes**

\* = Complications that were experienced by <10 patients.

**a** = Adjusted for observed differences in patient characteristics, such as age, sex and comorbid conditions (Attachment 5d 'El-Chami 2024a\_CED Protocol').

**b** = The assessment group was unable to find any explanation as to why the subtotals and totals do not add up.

RDs, RRs and associated CIs were calculated based on n/Ns which were estimated using the percentages provided in the post hoc analyses (weighted estimates of the logistic model) (RevMan v5.4).

**Bold** denotes statistical significance.

#### **Source**

Attachment 8 'Results of the post hoc subgroup analyses Micra AV CED'.xlsx

### **Chronic complications (2 years)**

Adjusted weighted cumulative incidence estimates indicated that fewer patients implanted with the Micra AV had chronic complications over the 2 years following surgery, compared with those receiving DC-TVPMs (4.8% versus 9.2%; hazard ratio [HR] 0.52, 95% CI 0.44, 0.61) (Table 8). This difference was mainly due to fewer incidences of device breakdown (1.4% versus 3.1%), dislodgment (0.5% versus 3.0%), device-related infection (0% versus 0.5%) and other mechanical failures (0.6% versus 1.5%) in the Micra AV group.

**Table 8 Chronic complications at 2 years in the Micra AV CED study (AV block without AF subgroup)**

	Observed events (%)	2-year weighted CIF estimates (95% CI)	Observed events (%)	2-year weighted CIF estimates (95% CI)	RRR (95% CI)	P value
<b>AVB without AF</b>	<b>Micra AV (N=3,902)</b>		<b>DC-TVPM (N=38,077)</b>		<b>Micra AV vs DC-TVPM</b>	
<b>Overall complications <sup>a</sup></b>	188 (4.8)	4.8% (4.6%, 5.2%)	3088 (8.1)	9.2% (8.8%, 9.7%)	48% (39%, 56%)	<b>&lt;0.0001</b>
Embolism and thrombosis	12 (0.3)	0.3% (0.2%, 0.3%)	76 (0.2)	0.3% (0.2%, 0.3%)	-7% (-106%, 44%)	0.8336
Thrombosis due to cardiac device	12 (0.3)	0.3% (0.2%, 0.4%)	79 (0.2)	0.3% (0.2%, 0.4%)	3% (-88%, 49%)	0.9355
Embolism due to cardiac device	*	*	*	*	16% (-577%, 90%)	0.869
Device-related complications	107 (2.7)	2.6% (2.5%, 2.7%)	2497 (6.6)	6.7% (6.6%, 6.8%)	62% (54%, 69%)	<b>&lt;0.0001</b>
Breakdown	51 (1.3)	1.4% (1.3%, 1.6%)	1025 (2.7)	3.1% (2.8%, 3.4%)	55% (39%, 67%)	<b>&lt;0.0001</b>
Dislodgement	19 (0.5)	0.5% (0.5%, 0.5%)	1094 (2.9)	3.0% (2.8%, 3.1%)	83% (74%, 89%)	<b>&lt;0.0001</b>
Other mechanical failure	26 (0.7)	0.6% (0.6%, 0.8%)	521 (1.4)	1.5% (1.3%, 1.7%)	56% (35%, 71%)	<b>&lt;0.0001</b>
Infection	0 (0)	0.0% (0.0%, 0.0%)	128 (0.3)	0.5% (0.4%, 0.6%)	100% (100%, 100%)	<b>&lt;0.0001</b>
Device pain	*	*	131 (0.3)	0.4% (0.3%, 0.5%)	66% (19%, 86%)	<b>0.0151</b>
Device stenosis	19 (0.5)	0.5% (0.4%, 0.7%)	150 (0.4)	0.6% (0.4%, 0.8%)	7% (-54%, 44%)	0.7673
Pocket complications	N/A	N/A	502 (1.3)	1.6% (1.4%, 1.8%)	NE	NE
Other complications	77 (2.0)	1.8% (1.8%, 1.9%)	591 (1.6)	1.8% (1.7%, 1.8%)	-5% (-36%, 19%)	0.7394
Pericarditis	58 (1.5)	1.5% (1.3%, 1.7%)	521 (1.4)	1.7% (1.5%, 1.9%)	9% (-25%, 34%)	0.5488
Hemothorax	24 (0.6)	0.7% (0.5%, 0.9%)	154 (0.4)	0.6% (0.5%, 0.8%)	-7% (-68%, 32%)	0.7594

**Abbreviations**

**AF** = atrial fibrillation, **AVB** = atrioventricular block, **CI** = confidence interval, **CIF** = cumulative incidence function, **DC-TVPM** = dual-chamber transvenous pacemaker, **N/A** = not applicable, **NE** = not estimable, **RRR** = relative risk reduction.

**Notes**

\* = Event occurred in <10 patients.

**a** = The assessment group was unable to find any explanation as to why the subtotals and totals do not add up.

**Bold** denotes statistical significance

**Source**

Attachment 8 'Results of the post hoc subgroup analyses Micra AV CED'.xlsx

## Reinterventions (2 years)

There was a statistically significant lower incidence of reinterventions over 2 years with the Micra AV, compared with DC-TVPMs (adjusted weighted cumulative incidence 3.3% versus 5.5%, HR 0.60, 95% CI 0.49, 0.72) (Table 9). This result was driven by lower rates of revisions (<0.3% versus 1.6%), system switch (leadless-to-transvenous or transvenous-to-leadless replacement; 0% versus 0.3%) and removal (<0.3% versus 0.6%) and the lack of lead-related reinterventions, which occurred in 1.3% of patients in the DC-TVPM cohort. However, replacements occurred more frequently with the Micra AV device than with DC-TVPMs (0.5% versus 0.1%, relative risk reduction -829%, 95% CI -1,894, -333). The applicant does not explain why the rate of device replacement was 5 times higher in the in the LPM group.

The higher rate of replacements in the first 2 years after implantation for the Micra AV, compared with DC-TVPMs, is pertinent from both economic and clinical perspectives. The Micra AV is not intended to be removed at the end of its life. It has been demonstrated that 3 Micra devices can be accommodated in the right ventricle of human cadaver hearts, but no more than 2 devices have been implanted in living patients.<sup>15</sup> This indicates an upper limit for the number of times Micra AV implants can be replaced, which may affect the functional utility timeline of the device if a second implant fails and necessitates a device switch over the longer term (i.e. after 2 years). It would be useful to know the reasons and timeline for these replacements, but this information was not reported in the submission.

**Table 9 Breakdown of the reinterventions at 2 years in the Micra AV CED study (AV block without AF subgroup)**

	Observed events (%)	2-year weighted CIF estimates (95% CI)	Observed events (%)	2-year weighted CIF estimates (95% CI)	RRR (95% CI)	P value
<b>AVB without AF</b>	<b>Micra AV (N=3,902)</b>		<b>DC-TVPM (N=38,077)</b>		<b>Micra AV vs DC-TVPM</b>	
Any reintervention	114 (2.9)	3.3% (3.1%, 3.6%)	1885 (5.0)	5.5% (5.1%, 5.9%)	40% (28%, 51%)	<b>&lt;0.0001</b>
Revisions	*	*	573 (1.5)	1.6% (1.4%, 1.8%)	93% (83%, 97%)	<b>&lt;0.0001</b>
Lead-related reinterventions	N/A	N/A	471 (1.2)	1.3% (1.2%, 1.5%)	NE	NE
Replacement	18 (0.5)	0.5% (0.4%, 0.8%)	18 (0.1)	0.1% (0.0%, 0.1%)	-829% (-1894%, -333%)	<b>&lt;0.0001</b>
System switch	0 (0)	0.0% (0.0%, 0.0%)	59 (0.2)	0.3% (0.2%, 0.4%)	100% (100%, 100%)	<b>&lt;0.0001</b>
Removal	*	*	167 (0.4)	0.6% (0.5%, 0.7%)	86% (56%, 96%)	<b>0.0009</b>
Upgrade to CRT	47 (1.2)	1.5% (1.3%, 1.7%)	603 (1.6)	1.9% (1.6%, 2.1%)	20% (-9%, 41%)	0.1596

### Abbreviations

**AF** = atrial fibrillation, **AVB** = atrioventricular block, **CED** = coverage with evidence development, **CI** = confidence interval, **CIF** = cumulative incidence function, **CRT** = cardiac resynchronisation therapy, **DC-TVPM** = dual-chamber transvenous pacemaker; **N/A** = not applicable, **NE** = not estimable, **RRR** = relative risk reduction.

### Notes

\* = Event occurred in <10 patients.

**Bold** denotes statistical significance

**Source** Attachment 8 'Results of the post hoc subgroup analyses Micra AV CED'.xlsx

<sup>15</sup> Omdahl P, et al. (2016). Right ventricular anatomy can accommodate multiple Micra Transcatheter Pacemakers. *Pacing Clin Electrophysiol* 39(4):393-397.

## **Pacemaker syndrome**

The Micra AV CED did not report pacemaker syndrome explicitly, which would likely have been captured in the rate of system revisions. Data from 2 single-arm studies were provided as supportive evidence, which indicated that pacemaker syndrome occurred in 0% to 0.3% of patients from 3 to 12 months after implantation with a Micra AV. However, at least 13% of patients had AF in each study, so it is unclear whether the rates of pacemaker syndrome reported in these studies apply to the proposed MBS population. There were no data available on the rate of pacemaker syndrome in patients receiving a DC-TVPM.

## **Interpretation and limitations of the safety data**

The main safety data are derived from a post hoc subgroup analysis of a single large non-randomised comparative study (low certainty evidence) (Table 10) in patients that are applicable to the proposed MBS population. The results indicated that the Micra AV is safer than DC-TVPMs with respect to rates of acute and chronic complications and reinterventions up to 2 years, mainly due to differences in rates of device-related events. However, the lack of information on the extent and severity of these device-related complications and how they were remedied made it difficult to determine how clinically important the differences are.

It is also unclear how the higher rate of replacements in the first 2 years after implantation for the Micra AV, compared with DC-TVPMs, affects the functional utility timeline of the device if a second implant fails and necessitates a device switch in an equivalently short time frame. Given that the Micra AV2 may be operative for at least 15 years, the lack of longer-term data is an issue that warrants consideration of ongoing data collection.








# **12. Comparative effectiveness**

## **All-cause mortality (30 days and 2 years)**

The 30-day mortality rate was higher with Micra AV implantation than with DC-TVPMs, in both unadjusted and adjusted analyses (adjusted analysis: 5.8% versus 3.0%; RR 1.94, 95% CI 1.69, 2.23) (Table 7). Within 2 years of surgery, 28.9% of patients implanted with the Micra AV and 14.6% of patients implanted with DC-TVPMs had died (HR 1.55, 95% CI 1.44, 1.68;  $p < 0.0001$ ). The adjusted cumulative incidence was 31.5% in the Micra AV group and 21.6% in the DC-TVPM group. As noted previously, it is possible that a proportion of patients who received the Micra AV in the subgroup analysis would have been ineligible for a DC-TVPM. This is an important confounding factor given that these patients tend to have a significantly higher rate of all-cause mortality than those who are eligible for either therapy.<sup>10</sup> It is also possible that the large imbalance in sample sizes between the 2 treatment groups (3,902 for Micra AV and 38,077 for DC-TVPM) may be an issue when controlling for baseline characteristics that are not independent of each other.

Even though the study used a weighted cohort of patients that differed with respect to device type but were similar with respect to 31 other baseline and encounter characteristics (preclusion for Micra AV was not considered), it is clear that there may still be confounding factors in the study. Consequently, the possibility that there are selection- and device-related effects influencing the result cannot be dismissed. Therefore, although the Micra AV resulted in a statistically significant higher 30-day and 2-year adjusted all-cause mortality rate than DC-TVPMs, it is unclear whether or to what extent the inclusion of patients in the LPM group who were ineligible for a DC-TVPM, and other potential confounding factors related to patient selection, affected this outcome.

**Table 10 Summary of evidence: Micra AV LPM versus DC-TVPMs**

Outcomes	Anticipated absolute effects* (95% CI)		Relative effect (95% CI)	№ of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Risk with DC-TVPM	Risk with Micra AV				
Micra AV CED study – ‘AVB without AF’ subgroup – adjusted analyses						
Acute complications (30 days)	104 per 1,000	87 per 1,000 (78 to 96)	<b>RR 0.83</b> (0.75 to 0.92)	41979 (1 non-randomised study)	 Low	Micra AV reduces acute complications (30 days).
Device-related complications (30 days)	41 per 1,000	15 per 1,000 (11 to 19)	<b>RR 0.36</b> (0.28, 0.47)	41979 (1 non-randomised study)	 Low	Micra AV reduces device-related complications (30 days).
All-cause mortality (30 days)	30 per 1,000	58 per 1,000 (51 to 67)	<b>RR 1.94</b> (1.69, 2.23)	41979 (1 non-randomised study)	 <sup>a</sup> Low	Micra AV increases all-cause mortality (30 days).
Chronic complications (2 years)	92 per 1,000	48 per 1,000 (42 to 57)	<b>HR 0.52</b> (0.44 to 0.61)	41979 (1 non-randomised study)	 Low	Micra AV reduces chronic complications (2 years).
Device-related complications (2 years)	67 per 1,000	26 per 1,000 (21 to 31)	<b>HR 0.39</b> (0.32 to 0.47)	41979 (1 non-randomised study)	 Low	Micra AV reduces device-related complications (2 years).
All-cause mortality (2 years)	216 per 1,000	315 per 1,000 (296 to 336)	<b>HR 1.55</b> (1.44 to 1.68)	41979 (1 non-randomised study)	 <sup>a</sup> Low	Micra AV increases all-cause mortality (2 years).
Reinterventions (2 years)	55 per 1,000	33 per 1,000 (27 to 40)	<b>HR 0.60</b> (0.49 to 0.73)	41979 (1 non-randomised study)	 Low	Micra AV reduces reinterventions (2 years).

#### Abbreviations

**AF** = atrial fibrillation, **AVB** = atrio-ventricular block, **CI** = confidence interval, **HR** = hazard ratio, **MD** = mean difference, **RR** = relative risk.

#### Notes

\* = The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

**a** = Possible confounding due to selection bias but unclear to what extent it affected the results.

⊕⊕⊕⊕ **High quality:** We are very confident that the true effect lies close to that of the estimate of effect.

⊕⊕⊕⊖ **Moderate quality:** We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

⊕⊕⊖⊖ **Low quality:** Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of the effect.

⊕⊖⊖⊖ **Very low quality:** We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect.

**Bold:** Statistically significant difference between groups.

## Quality of life

The Micra AV CED study did not report on QoL outcomes, so data from the prior MSAC Application 1672 on the Micra VR LPM compared with single-chamber transvenous pacemakers were provided. One of these supportive studies reported statistically significant differences in favour of LPMs relative to transvenous pacemakers at 6 months with respect to physical functioning, role physical, mental health and physical component summary scores. The other study reported statistically significant differences in favour of the LPM with respect to general health, vitality, social function, emotional wellbeing and the mental component summary scores. There was no reference made to the minimal clinically important differences for these measures among patients with heart conditions.

However, using QoL outcomes from the prior MSAC Application 1672 is appropriate only for the immediate aftercare period when healing of the generator pocket imposes restrictions on range of motion in the upper body and recovery. QoL outcomes beyond this period are likely to reflect not only patient comfort and activity restrictions related to device function, but also any effects of the devices on bradycardia symptoms, such as exercise capacity, shortness of breath, fatigue, dizziness and memory problems. Also, there are significant differences between the patients receiving LPMs in the Micra VR CED and Micra AV CED studies with respect to baseline rates of AF and other characteristics that are likely to affect QoL outcomes. It should also be noted that the evidence from the 2 studies was deemed to be of low certainty in the prior MSAC assessment. Therefore, given these issues and the differences in function between the Micra AV and VR, QoL outcomes from the Micra VR CED are not generalisable to the proposed MBS population—certainly not beyond the initial 4- to 6-week recovery phase—which precludes any definitive conclusions regarding QoL outcomes for the Micra AV.

## Technical performance

The Micra AV CED study did not report data on AV synchronicity or battery life.

A single modelling study of the Micra AV2 device projected a median battery life of 15.6 years (interquartile range 13.8, 18.7).<sup>16</sup> The study included patients with AV block, but it was unclear how many had normal sinus function or AF, and survival projections were based on data from patients receiving their first Medtronic dual-chamber pacemaker in the year 2000. Thus, the modelling of sinus rate variability may not be an accurate reflection of how the device would function in the proposed MBS population, and real-life comparative data are lacking.

Three supportive single-arm studies provided data on AV synchronicity. With optimal programming, resting and ambulatory AV synchronicity of 84.1% (95% CI 78.3, 88.6) and 82.6% (95% CI 75.8, 87.7) was achieved by the Micra AV.<sup>12</sup> Additional analysis of these data to simulate the function of the Micra AV and AV2 devices in virtual patients found that the Micra AV2 achieved an AV synchronicity of more than 70% in 90% of patients (27/30), compared with 43% (13/30) of patients with the Micra AV ( $p < 0.001$ ).<sup>16</sup> A third study found a median AV synchrony index of 79.4% in those paced  $>90\%$  with the Micra AV.<sup>17</sup> However, 2 of these studies included patients with AF (13%), and in one study it was unclear how many patients had normal sinus

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<sup>16</sup> Leal M, et al. (2024). Device longevity and AV synchrony algorithm modeling of a leadless pacemaker 1 family: a virtual patient analysis.

<sup>17</sup> Garweg, C., et al. (2024). A leadless ventricular pacemaker providing atrioventricular synchronous pacing in the real-world setting: 12-month results from the Micra AV post-approval registry. *Heart Rhythm* 21(10):1939-1947.

function or AF. Since these data are derived from single-arm studies, they cannot provide evidence on the effects of the Micra AV relative to DC-TVPMs for AV synchronicity.

### **Interpretation and limitations of the effectiveness data**

The main effectiveness data are derived from a post hoc subgroup analysis of a single large non-randomised comparative study (Table 10) in patients that are applicable to the proposed MBS population. This constituted low certainty evidence because it was likely that the LPM group included patients who were ineligible to receive a DC-TVPM (1 in 4 in the overall CED study LPM cohort). This selection bias potentially confounds the data in a way that is not necessarily offset by the propensity score matching method used to correct for the many other differences between the 2 treatment groups at baseline. Also, the DC-TVPM arm of the study represents retrospective data collection, a factor that would normally lead to downgrading in GRADE.

The results indicated that the implantation of a Micra AV results in higher all-cause mortality for up to 2 years, compared with DC-TVPMs. No comparative data was available for cardiovascular or procedure-related mortality, exercise capacity, patient satisfaction, implant success and failure rates and differential outcome by patient characteristics. The lack of cardiovascular and procedure-related mortality is problematic as it is unclear how many of the deaths in each treatment group were directly attributable to device function.

Despite using a weighted cohort of patients that were similar with respect to 31 baseline and encounter characteristics (preclusion for Micra AV was not considered), uncontrolled confounding factors may influence these results. For example, the large imbalance in sample sizes between the 2 treatment groups may be an issue when controlling for baseline characteristics that are not independent of each other. Also, it is possible that a proportion of patients who received the Micra AV in the subgroup analysis would have been ineligible for a DC-TVPM, and it is unclear whether or to what extent the inclusion of these patients in the LPM group confounded the outcomes. While it is possible that these factors skewed the mortality results in favour of DC-TVPMs, the possibility that there are other device-related effects influencing this result cannot be dismissed. The lack of mortality data beyond 2 years after surgery is an issue that warrants consideration of ongoing data collection given the projected longevity of the Micra AV device.

Quality of life, battery life and AV synchronicity were addressed with supportive evidence only, most of which was derived from single-arm studies in populations or devices (the Micra VR) that were not directly applicable to the MBS proposal.

It should be noted that the bulk of the evidence pertains to the Micra AV device, whereas the Micra AV2 will be used in Australia henceforth. Since the devices are identical in size, shape, mass, appearance, design and implant procedure, this is unlikely to affect safety outcomes. However, some effectiveness outcomes could be improved due to the enhanced atrial sensing and algorithms of the Micra AV2.

### **Clinical claim**

The clinical claim made by the applicant is that, compared with DC-TVPMs, the use of a Micra AV results in non-inferior effectiveness (all-cause mortality), inferior technical performance with respect to AV synchronicity and superior health-related QoL, as well as superior safety with respect to rates of acute and chronic complications and reinterventions. While the evidence provided supports the claim of superior safety, it does not support the claims of non-inferior effectiveness (all-cause mortality), inferior technical performance (with respect to AV synchronicity) or superior health-related QoL.



Results from one large non-randomised study indicate that patients who received a Micra AV for AV block in the absence of AF experienced significantly fewer complications (including device-related complications) and reinterventions at 2 years, compared with DC-TVPMs (low certainty evidence). However, the all-cause mortality rates are significantly higher following Micra AV implantation at 30 days and 2 years. Given the low certainty of the evidence, it is unclear to what degree this result represents confounding or selection- or device-related effects. Very limited data on QoL from studies on patients receiving a similar device (Micra VR) suggested that physical and mental functioning was better in those receiving an LPM device, compared with DC-TVPMs, in the postoperative recovery period up to one month following surgery. This is most likely due to the shorter period of activity restriction and recovery required for LPM recipients than for patients receiving DC-TVPM (approximately 24 hours versus 4 to 6 weeks). However, these patients were not representative of the proposed MBS population because of the large differences between the LPM patients in the Micra VR studies and the Micra AV CED study subgroup with respect to baseline rates of AF, congestive heart failure, chronic obstructive pulmonary disease and other characteristics likely to affect QoL outcomes. The lack of comparative data on the technical performance of the Micra AV in terms of AV synchrony and battery life precludes any definitive conclusions on these aspects.

### **13. Economic evaluation**

A cost-utility analysis (CUA) comparing the Micra AV LPM to DC-TVPM was performed based on the clinical claim of superior safety and non-inferior effectiveness. This analysis adapted the March 2022 CUA model developed for single-chamber LPM versus Micra VR pacing (MSAC Application 1672) to assess the Micra AV LPM. The model was structured to capture and evaluate the costs and health outcomes associated with the Micra AV and DC-TVPM over a time horizon of 16 years (i.e. estimated battery life of the Micra AV LPM). An Australian healthcare system perspective was taken, and a Markov model was used, including alive and dead health states. Most inputs from the original model were retained and applied to the updated model. However, complication risks and baseline utility values were revised based on evidence from the literature. A stepped approach was applied to present results over a model duration of 2 years to 16 years, and different quality-adjusted life year (QALY) transformations. Table 11 summarises the economic evaluation and an overview of the model parameters.

**Table 11 Summary of the economic evaluation**

Component	Description
Perspective	Healthcare system perspective
Population	Patients who are indicated for permanent pacing for the treatment of bradycardia due to paroxysmal or permanent high-grade AV block and who are in sinus rhythm
Comparator	DC-TVPM (i.e. the conventional strategy)
Type(s) of analysis	Cost-utility analysis
Outcomes	Quality-adjusted life years, life years
Time horizon	16 years (expected battery life of the Micra AV)
Computational method	Markov analysis
Generation of the base case	Modelled analysis Extrapolation of the within-trial risk estimates is presented in a stepped approach
Health states	Alive Dead
Cycle length	Annual
Transition probabilities / clinical events <sup>a</sup>	Infection (fatal and non-fatal) Revision Lead-related reintervention Replacement Removal
Discount rate	5% for both costs and outcomes
Software	Excel

**Abbreviations**

**AV** = atrioventricular block, **DC-TVPM** = dual-chamber transvenous pacemaker, **SND** = sinus node dysfunction.

**Notes**

**a** = The only modelled clinical events that trigger a transition to a 'Dead' state are fatal infection and other cause death (as informed by the Australian life table). Other clinical events are associated with transient cost/QoL implications without triggering any health state transitions.

The ADAR base-case analysis is considered appropriate and robust. The assumptions, methodology and parameters, by and large, align with the available evidence and practice. Uncertainties associated with the utility inputs and cost comparisons, including parameter variability and model assumptions, are discussed in the subsequent sections.

**Clinical inputs**

Complication risks, including infection, revision, lead-related reintervention, replacement and removal, were derived from the CED study focusing on the subgroup of AV block and normal sinus rhythm. Both first- and second-year risks were generally lower for LPM compared to DC-TVPM (except for 'replacement'), aligning with the clinical findings that LPM had a significantly lower incidence of acute, chronic and device-related complications, as well as reinterventions. The second-year risk was used as the annual rate for the subsequent years throughout the model duration. Mortality rates, however, were assumed to be the same across both arms. Mortality due to infection was informed by Sohail (2015), while all-cause mortality was based on Australian lifetables (Australian Bureau of Statistics). Although the clinical review indicated that LPM may increase all-cause mortality within 30 days and at 2 years, this finding was not used to inform the economic model inputs due to the low certainty of the evidence.

## **QoL inputs**

Baseline utility values were sourced from Chinitz (2023) and were identical between arms. Short-term and long-term disutility were modelled using data from Palmisano (2021) and applied exclusively to the DC-TVPM arm. Short-term disutility was applied for the first model cycle, primarily attributed to post-implantation physical restrictions and discomfort. Long-term disutility, reflecting the ongoing impact of lead or pocket, was assumed to apply to each cycle. Disutilities due to complications were applied per event and were equal across both arms. Infection-related disutilities were informed by Wilkoff (2020), while disutilities were same for other complications (i.e. revision, lead-related reintervention, replacement and removal) and based on Palmisano (2021).

## **Cost inputs**

Cost estimates for implantation procedures were calculated based on medical devices, professional services (MBS fees), and hospital stays. Management of complications used per event costs. The cost of managing an infection event was identical for both arms, based on Roder (2019), but the higher frequency of infections in the DC-TVPM arm led to greater overall costs. For other complications, management costs were calculated by adding an extra length of stay (LOS), with (for replacement only) or without the inclusion of the device fee. These costs were the same regardless of the complication types.

## **Results**

According to the ADAR submission, the base case results were derived from a stepped model analysis. The effects of model duration and QALY transformations were examined in a stepped manner to assess the impact on the model results (Table 12). The findings highlighted that the model duration significantly impacts the outcomes. This is primarily because the high intervention cost is a one-time cost incurred at baseline, while the ongoing benefits accrue gradually over time.

**Table 12 Results of the stepped economic analysis**

Step	Micra AV	DC-TVPM	Increment	ICER
Step 1 – Model duration of 2 years (CED trial maximum follow-up), all utility/disutility inputs captured				
Costs	\$redacted	\$14,395.08	\$redacted	
QALYs	1.5972	1.5582	0.0390	\$redacted
Step 2 – Model duration of 3 years (extrapolation beyond the CED data), all utility/disutility inputs captured				
Costs	\$redacted	\$14,509.32	\$redacted	
QALYs	2.3060	2.2616	0.0444	\$redacted
Step 3 – Model duration of 5 years (extrapolation beyond the CED data), all utility/disutility inputs captured				
Costs	\$redacted	\$14,711.61	\$redacted	
QALYs	3.5538	3.4993	0.0545	\$redacted
Step 4 – Model duration of 10 years (extrapolation beyond the CED data), all utility/disutility inputs captured				
Costs	\$redacted	\$15,077.58	\$redacted	
QALYs	5.7674	5.6935	0.0739	\$redacted
Step 5 – Model duration of 16 years (extrapolation beyond the CED data), all utility/disutility inputs captured (= base case)				
Costs	\$redacted	\$15,296.65	\$redacted	
QALYs	7.0218	6.9355	0.0863	\$redacted
Step 6 – Model duration of 16 years (extrapolation beyond the CED data), capture complication-related impacts only				
Costs	\$redacted	\$15,296.65	\$redacted	
QALYs	7.0218	7.0052	0.0166	\$redacted
Step 7 – Model duration of 16 years (extrapolation beyond the CED data), capture complication-related & post-procedural impacts only				
Costs	\$redacted	\$15,296.65	\$redacted	
QALYs	7.0218	6.9753	0.0465	\$redacted

**Abbreviations**

**AV** = atrioventricular, **CED** = coverage with evidence development, **DC-TVPM** = dual-chamber transvenous pacemaker, **ICER** = incremental cost-effectiveness ratio, **QALY** = quality-adjusted life year.

**Note**

Multiple outcomes may be informative for MSAC decision-making within each step.

The values highlighted in red were updated during the commentary to correct a calculation error. No changes were made to the model.

In the base-case model results (Table 13), where all utility/disutility inputs were captured, Micra AV demonstrated an average gain of 0.0863 QALYs compared to DC-TVPM, resulting in an incremental cost-effectiveness ratio (ICER) of \$redacted per QALY gained. ESC noted that the base-case results for Micra AV yielded an ICER that was higher than the base-case ICER for the Micra VR in Application 1672 (Table 14).

**Table 13 Results of the economic evaluation**

Parameter	Micra AV	DC-TVPM	Increment
Costs <sup>a</sup>	\$redacted	\$15,296.65	\$redacted
QALYs	7.0218	6.9355	0.0863
Incremental cost per QALY gained			\$redacted

**Abbreviation**

AV = atrioventricular, DC-TVPM = dual-chamber transvenous pacemaker, QALY = quality-adjusted life year.

**Note**

a = Both costs for implantation and management of complications are captured in the base case.

**Table 14 Micra VR base-case results<sup>#</sup> (12-year model duration) (MSAC application 1672)**

Parameter	Micra VR	TVPM	Increment
Costs	\$redacted <sup>#</sup>	\$7,997	\$redacted
QALYs	6.2689	6.1858	0.0832
Incremental cost per QALY gained			\$redacted

**Abbreviation**

VR = ventricular, TVPM = transvenous pacemaker, QALY = quality-adjusted life year.

**Note**

<sup>#</sup> base-case results adapted to include a redacted% reduction in the proposed Micra VR device price to \$10,083, as noted by MSAC in the Public Summary Document for MSAC Application 1672

## Uncertainty analysis

Key drivers of the model are summarised in Table 15.

There are uncertainties associated with the model inputs and evidence gaps, including the model duration. A stepped sensitivity analysis was conducted in the ADAR, varying the model duration from 2 to 16 years. The maximum duration of 16 years, based on the estimated battery life, was highly uncertain, due to the study reporting data for a minimum of 6 months only. The resulting ICERs are sensitive to this assumption, as detailed in [Table 12](#).

The absence of lead and pocket was assumed by the ADAR to improve the long-term QoL in patients with Micra AV, although there is little evidence to support this. This assumption has been shown to have a key impact on the overall results, accounting for 46% of the total QALY benefits.

**Table 15 Key drivers of the model**

Description	Method/value	Impact Base case ICER: \$redacted/QALY gained
Extrapolation	Re-estimation of costs and outcomes continued beyond 2 years for up to 16 years, the expected battery life of the Micra AV LPM predicted by supportive evidence. There are uncertainties around this extrapolation, as the expected median battery life of 15.6 years of the Micra AV LPM was predicted using virtual patient simulations, rather than real-world observational data. These simulations were based on real-world pacing parameters derived from a deidentified CareLink	High, favours Micra AV Use of a stepped approach decreased the ICER from \$redacted/QALY gained for 2-year horizon to \$redacted/QALY gained for 16-year horizon (base case). A significant amount of QALYs gained (0.0390/0.0863, 45.2%) occurred in the first 2 years.

Description	Method/value	Impact Base case ICER: \$redacted/QALY gained
	analysis of 999 Micra AV patients. <sup>18</sup> The minimum device implantation time was 6 months. It is also noted that the TVPM appears to have a shorter expected battery life (approximately 10–12 years) <sup>19 20</sup> compared to the LPM. As a result, patients implanted with the TVPM may require a device replacement due to battery failure within the 16-year time horizon, potentially leading to additional impact on costs and QALYs.	
Ongoing QoL impact due to TVPM	The long-term impact on QoL mainly due to the absence of lead and pocket, but there is no clear evidence to support it. The same disutility value from the March 2022 CUA model was applied to this model and also applied to DC-TVPM only, equivalent to a patient experiencing approximately one month of post-procedural QoL decrement (0.0608 ÷ 12). Compared with TVPM, to what degree the AV improving QoL remains unclear.	High, the direction is unclear If limiting the ongoing impact of DC-TVPM to 2 years, the ICER could reach as high as \$redacted/QALY gained; while double the disutility for DC-TVPM resulted in the ICER decreasing to \$redacted/QALY gained.
Post-procedural disutility	The -0.0304 disutility was derived from Palmisano (2021). The submission selected this study over Cabanas-Grandio (2019) to derive the estimated disutility for TVPM because it used propensity score matching.	High, the direction is unclear Doubling the disutility value for DC-TVPM reduced the ICER to \$redacted/QALY gained, while removing it entirely increased the ICER to \$redacted/QALY gained.
Infection cost	The base-case analysis used an inflation-adjusted cost (\$125,630) of \$98,097 from an Australian costing study, <sup>21</sup> a retrospective review of hospital records for CIED infections in Geelong, Victoria. A lower estimate of \$89,273 from unpublished Medtronic studies, which rely on expert inputs and public unit costs, supports the base-case results. However, the small numbers in the Roer 2019 cohort (41 admissions for 21 cases suffering from CIED infections) create uncertainty. Additionally, it is important to note that average number of admissions was 2 per infection, potentially doubling the associated costs.	Moderate, favours DC-TVPM If the cost of infection treatment is doubled, the ICER was calculated to be \$redacted/QALY gained.
Infection mortality	A 12-month mortality rate of 36% for patients with infections was used in the base case, based on Sohail 2015, <sup>22</sup> with mortality risk reverting to baseline after 12 months. This was applied to DC-TVPM, as the infection rate for LPM was zero.	Moderate, favours Micra AV When infection mortality was reduced to one-fourth (9%), the ICER rose to \$redacted/QALY gained; if infection mortality was excluded, the ICER increased further to \$redacted/QALY gained.

<sup>18</sup> Leal M, et al. (2024). Device longevity and AV synchrony algorithm modeling of a leadless pacemaker 1 family: aA virtual patient analysis.

<sup>19</sup> Moerke, C, Wolff, A, Ince, H, Ortak, J & Oner, A 2022, 'New strategies for energy supply of cardiac implantable devices', *Herzschrittmacherther Elektrophysiol*, vol. 33, no. 2, pp. 224-31.

<sup>20</sup> Munawar, DA, Mahajan, R, Linz, D, Wong, GR, Khokhar, KB, Thiagarajah, A, Kadhim, K, Emami, M, Mishima, R, Elliott, AD, Middeldorp, ME, Roberts-Thompson, KC, Young, GD, Sanders, P & Lau, DH 2018, 'Predicted longevity of contemporary cardiac implantable electronic devices: A call for industry-wide "standardized" reporting', *Heart Rhythm*, vol. 15, no. 12, pp. 1756-63.

<sup>21</sup> Roder, C, Gunjaca, V, Otome, O, Gwini, SM & Athan, E 2020, 'Cost and Outcomes of Implantable Cardiac Electronic Device Infections in Victoria, Australia', *Heart Lung Circ*, vol. 29, no. 7, pp. e140-e6.

<sup>22</sup> Rizwan Sohail, M, Henrikson, CA, Jo Braid-Forbes, M, Forbes, KF & Lerner, DJ 2015, 'Increased long-term mortality in patients with cardiovascular implantable electronic device infections', *Pacing Clin Electrophysiol*, vol. 38, no. 2, pp. 231-9.

Description	Method/value	Impact Base case ICER: \$redacted/QALY gained
Complication risks	The complication risks were taken from the CED study for AV block and normal sinus rhythm subgroup (2-year follow-up), so it is unclear that the model correctly extended the same risk rate over a device lifetime.	Moderate, favours Micra AV Not considering the risks after 2 years increased the ICER to \$redacted/QALY gained. However, evidence from long-term studies supported that complication risks extend beyond the initial 2 years post-implantation and were sustained or even increased over time (as detailed in Section 3A.2.4 in the ADAR document).

#### Abbreviations

AV = atrioventricular, CED = coverage with evidence development, CIED = cardiovascular implantable electronic device, CUA = cost-utility analysis, DC-TVPM = dual-chamber transvenous pacemaker, ICER = incremental cost-effectiveness ratio, LPM = leadless pacemaker, QALY = quality-adjusted life year, QoL = quality of life.

The results of key univariate sensitivity analyses are summarised in Table 16. Sensitivity analysis results for the time horizon were previously reported in Table 12 and are therefore not included here.

**Table 16 Sensitivity analyses**

Analyses	Incremental cost	Incremental QALY	ICER
Base case	\$redacted	0.0863	\$redacted
Ongoing QoL impact due to TVPM (base case -0.0051 per year to the model end)			
50%	\$redacted	0.0664	\$redacted
25%	\$redacted	0.0598	\$redacted
200%	\$redacted	0.1260	\$redacted
-0.0051 per year for 2 years	\$redacted	0.0579	\$redacted
-0.0051 per year for 5 years	\$redacted	0.0687	\$redacted
Post-procedural disutility (base case -0.0304)			
50%	\$redacted	0.0725	\$redacted
200%	\$redacted	0.1137	\$redacted
Taken out	\$redacted	0.0588	\$redacted
Infection cost (base case \$125,630)			
200%	\$redacted	0.0863	\$redacted
Infection mortality (base case 36%)			
25%	\$redacted	0.0729	\$redacted
Taken out	\$redacted	0.0703	\$redacted
Complication risks			
No risks after 2 years	\$redacted	0.0800	\$redacted
Pre-ESC response: TV-PM battery depletion/ replacement at 11 years	\$redacted	0.0863	\$redacted

#### Abbreviations

ICER = incremental cost-effectiveness ratio, QALY = quality-adjusted life year, TVPM = transvenous pacemaker.

## 14. Financial/budgetary impacts

The financial impact analysis took a market share approach. The number of DC-TVPM implants was estimated based on claims for MBS item 38356, extrapolated over the analysis period by assuming a linear growth trend. The number of eligible patients was derived from these estimates, based on the assumption that 35% of projected DC-TVPM implant procedures would be in patients who meet the proposed eligibility criteria for Micra AV. This assumption was based on characteristics of a Department of Veterans' Affairs cohort who received a pacemaker between 2005 and 2014.<sup>23</sup> It was estimated that the uptake of Micra AV would be **redacted**% of the eligible patient population in 2025 (Year 1), growing to **redacted**% by 2030 (Year 6).

A new item is requested for transcatheter insertion of Micra AV based on MBS item 38372 (current fee \$859.35, \$644.55 at 75% benefit). Replacement and removal will use the same respective items for the Micra VR (38373 and 38374; costs identical to 38372). Costs of Micra AV will replace the costs of DC-TVPM, which includes MBS item 38356 for insertion, replacement or removal of lead and MBS item 38353 for insertion, replacement or removal of pacing device. MBS item 60503 for fluoroscopy was included once as a co-claimed item for both procedures. It was unclear whether the financial/economic considerations, or both, included the relevant anaesthesia costs for the insertion procedure. The applicant may wish to clarify the type and costs of anaesthesia required for the procedure. A summary of the cost inputs included in the financial analysis is provided in Table 17.

**Table 17 Cost inputs included in the financial impact analysis**

Cost category	Micra AV LPM		DC-TVPM	
MBS costs	Transcatheter insertion (100% fee)	\$859.35	Insertion of lead (item 38356; 100% fee)	953.90
	Fluoroscopy (item 60503; 100% fee)	\$33.35	Insertion of pacing device (item 38353; 100% fee)	\$291 × 50% = \$145.50 <sup>a</sup>
			Fluoroscopy (item 60503; 100% fee)	\$33.35
<i>Total MBS costs (75% benefit)</i>		\$669.53		\$849.56
Other resource use	Prosthesis costs	\$ <b>redacted</b>	Prosthesis cost for leads (PL 08.08.09)	\$6,870
			Prosthesis for pacing device (PL 08.04.04)	\$1,072
	2-day hospital stay	\$4,552	2-day hospital stay	\$4,552
<i>Total cost per patient (75% benefit)</i>		\$ <b>redacted</b>		\$13,343.56

**Abbreviations:**

**DC-TVPM** = dual-chamber transvenous pacemaker, **LPM** = leadless pacemaker, **MBS** = Medicare Benefits Schedule, **PL** = Prescribed List.

**Notes:**

**a** = Current MBS fee of \$291 adjusted for multiple operation rule x 50%

**Source:**

Compiled during the commentary using data from Table 59 and Table 60 of the ADAR.

<sup>23</sup> Gillam, MH, Pratt, NL, Inacio, MC, Shakib, S, Sanders, P, Lau, DH & Roughead, EE 2018, 'Rehospitalizations for complications and mortality following pacemaker implantation: A retrospective cohort study in an older population', *Clinical cardiology*, vol. 41, no. 11, pp. 1480-6.



The total market-size estimate based on MBS item 38356 includes retrieval as well as replacement items. The submission, therefore, suggests the estimates presented are inclusive of the newly requested insertion item and the 2 existing items for retrieval and replacement (items 38373 and 38374), which carry the same MBS fee. However, the submission also notes that most Micra AV-related procedures during the first 6 years would be expected to be for the insertion procedure. However, claiming of MBS item 90300 by a cardiothoracic surgeon is also required >4 weeks after the insertion of a leadless pacemaker when an interventional cardiologist is undertaking the services under items 38373 and 38374 for retrieval or replacement. As of November 2024, no claims for MBS items 38373 or 38374 were associated with the Micra VR device.

The applicant assumed fewer costs of complications for Micra AV than DC-TVPM, and the associated costs were excluded from the analysis. No sensitivity analysis was conducted.

The financial implications to the MBS resulting from the proposed listing of the Micra AV LPM are summarised in Table 18. The submission calculated the new item to have a cost-saving impact on the MBS. The projected cost saving was \$redacted in 2025 and grew linearly to \$redacted in 2030 at 75% benefit.

**Table 18 Net financial implications of Micra AV LPM to the MBS**

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
<b>Estimated use and cost of Micra AV LPM</b>						
Number of people eligible for Micra AV LPM	3,217	3,308	3,398	3,489	3,580	3,670
Number of people who receive a Micra AV LPM	redacted	redacted	redacted	redacted	redacted	redacted
LPM costs, proposed MBS item, 75% benefit	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Fluoroscopy costs (MBS item 60503), 75% benefit	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Cost to the MBS	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
<b>Change in use and cost of DC-TVPM</b>						
Change in use of DC-TVPM	redacted	redacted	redacted	redacted	redacted	redacted
DC-TVPM costs (MBS items 38356 and 38353), 75% benefit	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Fluoroscopy costs (MBS item 60503), 75% benefit	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Change in MBS cost for DC-TVPM	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
<b>Net financial impact to the MBS</b>	<b>\$redacted</b>	<b>\$redacted</b>	<b>\$redacted</b>	<b>\$redacted</b>	<b>\$redacted</b>	<b>\$redacted</b>

#### Abbreviations

**DC-TVPM** = dual-chamber transvenous pacemaker, **MBS** = Medicare Benefits Schedule, **LPM** = leadless pacemaker.

#### Notes

MBS costs are calculated as a 75% benefit of the listed fee.

One of the concerns is the number of eligible patients was estimated based on a veteran population,<sup>23</sup> of which characteristics differ from the population of interest. The estimate of 35% of DC-TVPM patients being eligible for the Micra AV was derived from 39% of DC-TVPM patients having AV block. In comparison, the Micra AV CED study reported that 47.6% of patients using DC-TVPM have AV block,<sup>11</sup> indicating that the number of eligible patients could be underestimated (although this includes patients with or without AF). Of the 110,558 DC-TVPM

patients in the Micra AV study, 38,077 (34.4%) had AV block without AF and were included in the ADAR's clinical analysis (ADAR Table 13, p58).

Another concern of the financial impact analysis is the uncertainty in the uptake of Micra AV. The uptake was estimated at **redacted**% of eligible patients in the first year in the ADAR text, with detailed reasoning. The **redacted**% figure is consistent with the estimation provided by 3 experts consulted by the applicant, who indicated that currently,  $\leq 5\%$  of patients with AV block in sinus rhythm are contraindicated for a transvenous option or have a very high clinical need for a leadless option. However, a Year 1 uptake rate of **redacted**% was used in the calculations.

The advisory board, which the applicant consulted with, indicated that they would only use Micra AV for patients with a clinical need for a leadless option; 3 clinical experts suggested that currently  $\leq 5\%$  of patients with AV block in sinus rhythm are contraindicated for a transvenous option or have a very high clinical need for a leadless option. Based on this assessment, a Year 1 uptake rate of **redacted**% is more plausible than **redacted**%. The **redacted**% starting point also aligns with historical data on Micra VR initial uptake, extracted from MBS item reports.<sup>24</sup> MBS item 38372 (available from November 2023) is currently used solely for Micra VR; its 10-month usage (Nov 2023 – Sep 2024) was 139 services. MBS item 38350 is used for the insertion, removal or replacement of transvenous leads associated with single-chamber pacemakers, the comparator of Micra VR. Its usage in the same period was 3,126 services. Based on these figures, the uptake of Micra VR was 4.26% in the first 10 months of listing. The Year 1 uptake of Micra VR was projected by the assessment group as unlikely to exceed **redacted**%. Reducing the Micra AV Year 1 uptake to **redacted**% reduces the estimated cost to the MBS of the proposed item over the 6 years by **redacted**%, while also reducing the estimated cost savings by **redacted**% (i.e. the net cost estimate becomes less negative). Nevertheless, the **redacted**% uptake rate may be considered the more conservative estimate for the current assessment. Of patients with AV block without AF from the Micra AV CED study included in the ADAR's clinical analysis, 9.3% received the Micra AV, while 90.7% received a DC-TVPM.

The market estimates, which were based on DC-TVPM usage, do not capture patients who are ineligible for DC-TVPMs, would otherwise receive a Micra VR, or currently have a Micra VR implant but might benefit from switching to the Micra AV. While only a small proportion of the overall eligible population, these subgroups appear to overlap with a large proportion of the predicted Micra AV LPM uptake in Year 1. While DC-TVPM costs in all patients offset Micra AV costs, these offsets may be irrelevant in a significant proportion of the projected cases. In some patients, a surgically implanted (epicardial) pacemaker or Micra VR may be the more appropriate comparator, with the DC-TVPM being the relevant comparator only in patients for whom dual-chamber transvenous pacing is an option but is not necessary for effective therapy. Across the entire Micra AV CED cohort, 23% of patients who received the LPM would have been ineligible for the DC-TVPM (it is unclear how many of these patients were in the AV block without AF subgroup analysed in the submission).<sup>10</sup> Expert advice received during the commentary suggests a switch from the Micra VR to the Micra AV could be considered if clinically significant symptoms of a lack of AV synchrony were problematic. However, it would be rare in practice (personal communication, expert cardiologist and electrophysiologist, 14 December 2024).

Additionally, the reason for the **redacted**% uptake estimate in Year 6 is not provided. The ADAR mentioned a large range in reported use of VDD pacing (i.e. pacing to the ventricle and sensing in both the atrium and ventricle), from 0% to 65.8% of all implantable cardiac devices. Given the wide range of adoption of VDD worldwide, and considering that LPM has advantages but lacks data supporting its long-term effects and acceptance, future uptake is uncertain.

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<sup>24</sup> Services Australia 2024, *Medicare Item Reports*, [http://medicarestatistics.humanservices.gov.au/statistics/mbs\\_item.jsp](http://medicarestatistics.humanservices.gov.au/statistics/mbs_item.jsp).

No breakdown of the costs and severity of complications also contributes to uncertainty. Although the total adjusted acute complication rate within 30 days was lower for patients implanted with a Micra AV compared to those who received a DC-TVPM (Table 7), there were differences in the types of acute complications that occurred. The adjusted complications at 2 years were also lower for patients implanted with a Micra AV than those who received a DC-TVPM (Table 8). The comparative severity and costs of the complications across arms is unclear.

The economic model accounted for infections, revisions, lead-related reinterventions, replacements and removals when costing complications, and reported higher complication costs associated with DC-TVPM. Considering this, the exclusion of complications costs may be conservative. Nevertheless, costs for surgical explantation, although likely rare according to the ADAR, were not captured in the modelling, and remain an area of uncertainty.

The real-world cost of the explantation of Micra AV is uncertain. The Public Summary Document (PSD) for MASC application 1672 has pointed out that explantation is unlikely due to clinicians' unwillingness to deal with the difficulty of removing encapsulated LPMS. The claim that the chamber can hold 3 devices is not supported; the supporting study referred to in the ADAR only mentioned 'up to 3 devices' as the submitter's claim<sup>25</sup>. According to the post hoc analysis, the 2-year replacement rate of Micra AV is 5 times that of DC-TVPM (2-year risks: 0.5% versus 0.1%, respectively). In the future, some patients may need explantation of multiple devices.

There is also concern about leakage beyond the proposed population. Micra AV can be used in broader patient groups than the targeted population. The population covered in Micra AV's ARTG listing includes patients with AV block with or without AF. Furthermore, in the Micra AV CED study, only 74% of patients who received a Micra AV device had AV block. The ADAR mentioned the market share of VDD has a wide range, up to 65.8% of total ICDs. Micra AV is a leadless VDD device, suggesting a potentially large leakage.

For the impact on other health resources, the submission estimated 2 days of hospital stay per procedure (\$4,552), identical to DC-TVPM (Table 17), expecting no financial impact (Table 1919). The cost of the medical device for AV LPMS has the major impact on private health insurers. The proposed cost of pacemakers and consumables for AV LPM is **\$redacted**, higher than unit costs of \$7,942.00 for DC-TVPM (Table 1717). The increased financial costs to health insurers are projected to be **\$redacted** in 2025, rising to **\$redacted** in 2030 (Table 19).

The overall financial impact to the healthcare system is projected to be **\$redacted** in 2025 to **\$redacted** in 2030.

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<sup>25</sup> Fagerlund BC, Harboe I, Giske L, Movik E, Ørjasæter IK, Tjelle TE. The Micra TM Transcatheter Pacing System, a leadless pacemaker, in patients indicated for single chamber ventricular pacemaker implantation: A single technology assessment from the Norwegian Institute of Public Health (Folkehelseinstituttet). Oslo: Norwegian Institute of Public Health, 2018.

**Table 19 Net financial implications of the proposed listing in terms of other hospital resources, prosthesis costs and total impact to the Australian healthcare system**

Parameter	Year 1	Year 2	Year 3	Year 4	Year 5
Hospital costs with Micra AV	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Change in hospital costs	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
<i>Net hospital costs</i>	\$0	\$0	\$0	\$0	\$0
Prosthesis costs with Micra AV	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
Change in prosthesis costs	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
<i>Net prosthesis costs</i>	\$redacted	\$redacted	\$redacted	\$redacted	\$redacted
<b>Overall net financial impact to Australian healthcare system</b>	<b>\$redacted</b>	<b>\$redacted</b>	<b>\$redacted</b>	<b>\$redacted</b>	<b>\$redacted</b>

**Notes**

Compiled during the commentary using data from Table 65, Table 66 and Table 67 of the ADAR.

In summary, the financial impact of the Micra AV on the MBS was estimated to be cost-saving. However, the amount of cost savings is uncertain. Overall, the major concerns include an underestimated number of eligible patients, overestimated Year 1 uptake, high uncertainty in the Year 6 uptake, uncertainty of costs for managing complications, and uncertainty of future explantation costs.

## 15. Other relevant information

Nil.

## 16. Key issues from ESC to MSAC

### Main issues for MSAC consideration

#### Clinical issues:

- The criteria for the eligible population should be more accurately defined, as well as the degree of atrioventricular synchrony (AVS) required vs ventricular pacing. Expert consensus is required to determine whether the population should be limited to patients in sinus rhythm, as this device can potentially be used for patients with paroxysmal atrial fibrillation (AF) or patients with AF awaiting reversion to sinus rhythm.
- There was no clinical comparison presented between the proposed intervention, Micra™ AV (atrioventricular), and the PASC-nominated secondary comparator relevant for some of the population, Micra™ VR (ventricular), to enable an assessment of their comparative safety and clinical effectiveness. ESC considered that additional data to make this comparison would be necessary to justify the greater Prescribed List (PL) benefit being sought for the Micra AV device relative to the Micra VR device, namely to justify supporting a higher PL benefit. ESC did not consider there to be sufficient evidence to demonstrate a meaningful difference in effectiveness between the Micra AV and the Micra VR.
- The application presented insufficient evidence related to the efficacy of Micra AV vs dual chamber transvenous pacemaker (DC-TVPM). Additional evidence regarding the specific predefined criteria for which Micra AV is appropriate and the predefined population specified for the device (younger age, prior VR leadless pacemaker, etc.) would be useful, in addition to the comparison of Micra VR vs Micra AV. The MBS item descriptor will require revisions to include these points once the evidence is available.

### **Economic issues:**

- There was no economic evaluation comparing Micra AV and Micra VR to enable an assessment of the relative cost-effectiveness of the higher benefit of Micra AV (\$redacted proposed PL benefit) versus Micra VR (current PL benefit of \$10,083).
- The applicant supplied a revised incremental cost-effectiveness ratio (ICER) to include replacement costs for DC-TVPM (after approximately 11 years), which reduced the ICER to \$redacted/QALY. ESC noted that the applicant submitted no updated model, and the ICER could not be independently verified. ESC considered that the impact of the time horizon in the updated ICER was inappropriately favourable to Micra AV by implying that Micra AV does not need replacing and, therefore the updated ICER is not informative for decision-making. ESC considered that additional sensitivity analyses across a range of time horizons that capture replacement costs for both DC-TVPM and Micra AV LPM would be more helpful for MSAC for interpreting the reliability of the ICER.

### **Financial issues:**

- The estimated ESC considered that the cost offsets for DC-TVPM substitution may not materialise, as clinical feedback indicates that ≤5% of atrioventricular block (AVB) patients are contraindicated for transvenous options.
- If Micra VR is also a relevant second comparator then the impact of the Micra AV on the Micra VR market share should also be considered.

### **ESC discussion**

ESC noted that this application from Medtronic Australasia seeks to facilitate the listing of the Micra™ AV (atrioventricular) device on the Prescribed List of Medical Devices and Human Tissue Products (PL). The applicant intends to apply for PL listing of the Micra AV device following MSAC consideration.

ESC acknowledged consultation feedback from 2 organisations. Hearts 4 Heart feedback was supportive, highlighting that a leadless pacemaker (LPM) is a suitable option for patients who would otherwise be restricted by the leads associated with traditional pacemakers, notably physically active people and those with cognitive disability, who could benefit from LPMs. LPM removes the risk of leads breaking or being pulled out, which can cause infections. Feedback from Abbott, whilst supportive in general terms of MBS items allowing patient access to leadless cardiac devices, argued that using DC-TVPM as the comparator was not appropriate due to limitations of the Micra AV, and that a more appropriate comparator for the proposed patient population would be a ventricular single-lead VDD pacemaker. However, ESC noted PASC advice that the use of VDD TVPM technology is no longer relevant in current Australian clinical practice as VDD TVPM devices are not listed on the PL and are no longer sold in Australia. ESC noted PASC's position maintaining DC-TVPM as the most appropriate comparator, given its availability and current clinical use in Australia.

Regarding the proposed population, ESC considered the populations that should be excluded as ineligible for Micra AV should be clearly defined in the proposed MBS item descriptor for percutaneous insertion rather than in an explanatory note, which is not subject to regulation. ESC first considered that the eligibility criteria should be more accurately defined in terms of the degree of atrioventricular synchrony (AVS) required vs ventricular pacing. ESC noted that the device cannot provide 100% AVS and that AVS becomes less reliable when patients' heart rates are above 100 beats per minute. Therefore, ESC considered the device most suitable for patients who are not physically active, such as older people with co-morbidities and restricted physical activity. ESC considered that the eligibility criteria should specify the age and heart rate of eligible patients, to ensure that the population is limited to those who would most benefit from the device.

ESC also considered that expert consensus may be informative in determining whether the population should be limited to patients with sinus rhythm, as this device can potentially be used for patients with paroxysmal atrial fibrillation (AF) or patients with AF awaiting reversion to sinus rhythm.

ESC agreed in principle with the amendments proposed to the MBS item descriptor by the department. However, it is considered that more prescriptive criteria are required to avoid clinical misinterpretation.

ESC noted that the proposed clinical management algorithm was appropriate.

ESC noted that existing MBS items for leadless pacemaker (LPM) – [38372](#) (insertion), [38373](#) (retrieval and replacement), [38374](#) (retrieval) and [38375](#) (explanation) – can be claimed for services associated with the use of the Micra AV device without amendment. However, ESC acknowledged that PASC had raised concerns about the broad nature of the MBS items proposed for use with the Micra AV and the potential for the device to be used beyond its intended population, which could lead to increased costs to the MBS. ESC also recognised that PASC considered the need for a new MBS item for the insertion of the device, specifying that patients must be in sinus rhythm. Additionally, ESC also acknowledged PASC's recommendation, including an explanatory note with the proposed MBS item to specify the patients for whom the device is not recommended (that is, patients with sinus bradycardia with or without chronotropic incompetence). ESC noted the PASC emphasis on creating a new item with a more restricted population if the Micra AV is listed on the PL with a greater benefit than the Micra VR. This application proposed a new MBS item for the insertion of a LPM providing AVS at the same fee as the current MBS item 38372 for insertion of Micra VR (\$859.35), and an explanatory note as per PASC advice. ESC noted no changes were proposed to the existing MBS items 38373, 38374, and 38375.

ESC also considered that a new MBS item would need to be created with a more restricted patient population than the related Micra VR. MSAC previously considered and supported the MBS listing of the insertion or removal of a permanent leadless pacemaker (Micra VR) for treating bradyarrhythmia that requires single-chamber ventricular pacing ([MSAC Application 1672](#)). ESC considered this would be important given the request to list Micra AV on the PL at a greater benefit than the VR model, but this request is not supported by data on the incremental effectiveness of the Micra AV compared to the Micra VR. Additionally, ESC noted that if Micra AV is listed on the PL, existing MBS item 38372 will need to be amended to restrict the use of this item only to patients where a sufficient degree of AVS is not required.

ESC noted that the proposed comparator is a standard dual chamber transvenous pacemaker (DC-TVPM). ESC noted that similar to single chamber TVPMs, Micra AV has traditional remote monitoring capabilities (via a physical monitor), but it is not capable of Bluetooth monitoring due to its small size. However, consistent with PASC, ESC considered that Micra VR was also a relevant secondary comparator because of the overlap in eligible population for the Micra AV and Micra VR for patients with paroxysmal or permanent high-grade AV block in the absence of atrial fibrillation.

ESC noted that the potential advantages of leadless pacing compared to conventional dual-chamber pacing are based on:

- Eliminating lead and pocket complications, thereby presenting advantages from a safety perspective.
- Reductions in pacemaker-related infections (mainly related to TVPM subcutaneous pocket and lead infections) which are a significant concern due to increased risk of

morbidity and mortality and the high cost to the healthcare system of treating a pacemaker-related infection.

- Improved quality of life (QoL) due to earlier return to activities of daily living and independence.
- The omission of pain, discomfort and aesthetic issues pertaining to the subcutaneous pocket required for a transvenous pacemaker (TVPM).

ESC noted that the pivotal study for the current application was a predefined post hoc subgroup analysis of the Micra AV 'coverage with evidence development' (CED) study. The study included a large non-randomised cohort which of 118,110 patients who had a Micra AV device or a DC-TVPM implanted. ESC noted that the study used US claims data and included a 24-month follow-up period. ESC noted that the post-hoc subgroup analyses were conducted to evaluate the effectiveness and safety of the Micra AV device versus DC-TVPM in patients with AV block (AVB) and who are in sinus rhythm (subgroup referred to as 'AVB without AF'; N = 41,979), as a proxy for the proposed population. Propensity score overlap weights were used to construct a weighted cohort of patients with different pacemaker types (i.e. LPM vs TVPM). However, ESC noted that patients receiving a LPM appeared to have more comorbidities than the DC-TVPM group, which was potentially a source of confounding which may have contributed to the higher all-cause mortality found in the LPM group compared to the DC-TVPM group.

ESC agreed with concerns regarding the weak evidence for superior safety, as it relied entirely on single-arm and real-world studies. ESC noted that both the Micra AV device and DC-TVPM have acute implantation risks. However, ESC acknowledged that LPM technology in general significantly reduces the risk of lead and pocket infection compared to DC-TVPM.

ESC further noted that the evidence base included 5 additional studies as supportive evidence reporting QoL outcomes. ESC noted that the Micra AV device significantly improves QoL related to aesthetics and thrombosis. However, these studies did not consider that unlike DC-TVPM, the Micra AV device does not require surgical excision and therefore patients may be able to be discharged following implantation either on the same or next day. ESC considered that this would have likely contributed to improved QoL compared to DC-TVPM. Additionally, ESC noted that there was selection bias within these studies, as patients who received Micra AV were ineligible for DC-TVPM.

ESC also noted issues with the evidence base, particularly the limited evidence for the Micra AV vs DC-TVPM comparator. There was no analysis of Micra AV vs the secondary comparator (Micra™ VR). ESC agreed with PASC advice that comparative clinical evidence should have been presented in the applicant-developed assessment report (ADAR) to identify additional benefit of the Micra AV device over the Micra VR model, especially if a greater PL benefit is sought for the Micra AV device. Furthermore, ESC noted that there is limited evidence regarding the efficacy of the Micra AV's sensing capability over DC-TVPM, its effectiveness in different population groups is not available, and the data has been extrapolated from studies with low sample sizes, which is suboptimal.

ESC noted that the economic evaluation was a cost-utility analysis, based on the clinical claims of superior safety and non-inferior efficacy (including mortality) and superior QoL. The time horizon was 16 years, based on the expected battery life of the Micra AV device. However, ESC noted discrepancy in the reported expected battery life: the PICO stated it was 8–13 years, while a single modelling study of the Micra™ AV2 device (included in the ADAR) projected a median life of 15.6 years. Additionally, ESC noted that the capability of the device to provide AVS pacing affects battery life (range of 8–15 years), and battery depletion requires implantation of another device. ESC requested the applicant address the effect of AVS pacing on the battery life of the device. ESC considered this should be incorporated in the economic model.

ESC noted that while the economic model had no major structural issues, it was based on uncertain clinical evidence. ESC raised concerns about the applicability of the QoL data and considered that it was reasonable to assume that Micra AV offers ongoing utility improvements over DC-TVPM due to the absence of leads and a chest pocket, despite the lack of supporting evidence. ESC noted from the applicant's pre-ESC response that MSAC had previously accepted maintenance of long-term QoL benefits for the leadless technology in its assessment of [MSAC Application 1672](#) (for single-chamber LPM vs Micra VR pacing), hence the applicant applied the same assumption in this application. Nonetheless, ESC suggested that sensitivity analyses were needed that focus on reducing QoL effectiveness. ESC also considered it was unclear whether disease progression and reversion to a conventional lead PM was incorporated into the economic model.

ESC noted that the model used a Markov analysis with two health states, adapting the cost-utility analysis model developed for MSAC Application 1672 to assess the Micra AV LPM. Most inputs were from the original model, with revisions made to the comparator risks and baseline based on literature. The base-case results from MSAC Application 1672 are provided in Table 14.

ESC noted that the stepped analysis was modelled over 16 years, with step 5 as the base case. The base case incremental cost-effectiveness ratio (ICER) was \$redacted per quality-adjusted life year (QALY). ESC noted that the commentary highlighted uncertainties regarding the 16-year extrapolation time, due to the estimated shorter battery life of DC-TVPM (10–12 years) potentially leading to earlier replacement costs and health outcomes. In the pre-ESC response, the applicant provided revised estimates that included replacement costs for DC-TVPM after approximately 11 years, reducing the ICER to \$redacted/QALY. ESC noted that the applicant did not submit an updated model and this ICER could not be independently verified. ESC noted the revised ICER accounts for the replacement costs of DC-TVPM after 11 years but does not consider the later replacement of Micra AV. Estimates for the battery life varied between 8-13 years for the Micra AV as noted in the PICO confirmation, and a median battery life of 15.6 years used by the ADAR for the Micra AV2 model. ESC considered that the selected time horizon of the updated ICER lacked face validity and therefore the updated ICER is not informative for decision-making. The cost advantage reflected in the 11th to 12th year may be temporary or inaccurate, and over a longer time horizon, both technologies would require replacement, potentially altering the ICER. ESC considered that additional sensitivity analyses across a range of time horizons that capture replacement costs for both DC-TVPM and Micra AV LPM would be useful to improve the robustness of the ICER.

ESC noted that a Markov trace was used for model validation, comparing the incidence of the modelled clinical events in the Micra AV and DC-TVPM cohorts over the 16-year analysis period. The traces crudely align with recent NSW data reporting a 1.3% rate of cardiac implantable electronic device-related infections at a median of 26 months follow-up.

ESC noted that the key drivers of the model were extension of the time horizon beyond 2 years to 16 years, the ongoing QALY difference vs DC-TVPM, and post-procedural disutility. These drivers changed the base case ICER by 18–49% in both directions. Notably, extending the timeline alone reduced the ICER from \$redacted/QALY over 2 years to \$redacted/QALY over 16 years. Infection cost, infection mortality and complication risks all had moderate impacts on the ICER. ESC considered that additional sensitivity analyses varying the utility weights would aid decision-making.

ESC noted PASC advice that insertion of a Micra VR device should be included as a secondary comparator if the applicant intends to seek a higher PL benefit for the Micra AV. ESC noted that the proposed higher PL benefit for Micra AV was not supported by the evidence or analyses presented in the ADAR.



ESC considered that the use of a market share approach to estimate the financial impacts was appropriate. The number of Micra AV device implantations was estimated based on the usage of [MBS item 38356](#) (insertion, removal or replacement of DC permanent transvenous electrodes), extrapolated over 16 years using a linear growth trend. ESC noted that 35% of DC-TVPM implants are projected to be used in patients who are also eligible for Micra AV, based on a Department of Veterans' Affairs (DVA) cohort (2005–2014). While ESC acknowledged concerns from the commentary about whether the DVA cohort was representative of the general population, ESC considered the cohort reasonable in the absence of other data. ESC noted that Micra AV uptake is estimated at **redacted**% of these eligible patients in year 1, growing to **redacted**% by year 6, though ESC considered these uptake rates to be uncertain. ESC noted that the estimated cost offsets for DC-TVPM substitution may not materialise, as clinical feedback suggests that ≤5% of AVB patients are contraindicated for transvenous options.

ESC noted that the net financial impact to the Medicare Benefits Schedule (MBS) was estimated in the ADAR to be a cost saving of **\$redacted** in year 1 increasing to a cost saving of **\$redacted** by year 6. The overall net financial impact to the Australian healthcare system was estimated by the ADAR to be **\$redacted** in year 1 increasing to **\$redacted** in year 5. ESC noted that if the Micra VR is also a relevant second comparator then the impact of the Micra AV on the Micra VR market share should also be considered.

ESC noted that the department suggested this application be reviewed by the Medical Devices and Human Tissue Advisory Committee (MDHTAC) Cardiovascular Expert Clinical Advisory Group (CVECAG) before MSAC consideration. ESC noted that the CVECAG may provide additional clinical expertise regarding the comparative clinical performance of the devices however, ESC considered that the current application should proceed to MSAC via the standard processes.

## **17. Applicant comments on MSAC's Public Summary Document**

Nil.

## **18. Further information on MSAC**

MSAC Terms of Reference and other information are available on the MSAC Website: [visit the MSAC website](#)