Medical Services Advisory Committee (MSAC) Public Summary Document

Application No. 1749 – Insertion of durable left ventricular assist device for use as destination therapy

Applicant: **Abbott Medical Australia Pty Ltd.**

Date of MSAC consideration: **29 November 2024**

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

1. Purpose of application

A resubmission requesting Medicare Benefits Schedule (MBS) listing for the insertion of durable left ventricular assist device (LVAD) as destination therapy (DT) in the management of refractory heart failure despite optimal medical management (OMM), was received from Abbott Medical Australia Pty Ltd by the Department of Health and Aged Care.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC supported the creation of a new MBS item for the insertion of durable LVAD for use as DT for patients with refractory heart failure who are not eligible for cardiac transplantation. MSAC considered that use of a LVAD had superior effectiveness compared to OMM. MSAC recalled that it previously deferred providing its advice and requested further information relating to the aftercare services needed following LVAD insertion, including a more informed estimate of aftercare costs. MSAC requested that the economic and financial analyses be revised with these updated costs and that the economic model inputs be updated as specified by MSAC (including the incorporation of device replacement costs other than for pump thrombosis).

MSAC noted from consultation feedback that the upper limit of contemporary aftercare costs within the first two years post LVAD implantation is approximately $39,130 per patient per year. MSAC considered that the revised economic evaluation which incorporated this upper limit of aftercare costs was broadly aligned with MSAC's previous advice. Although the incremental cost-effectiveness ratio (ICER) was high, MSAC considered it to be acceptable for the small proposed patient population who currently have a poor prognosis and a lack of effective alternative treatments. MSAC noted that the revised financial analysis did not include device replacement costs for reasons other than pump thrombosis but based on consultation feedback including from Australian LVAD implant centres, MSAC considered the rate of LVAD replacement would be very low and was unlikely to have a significant effect on the total financial impact. Given that the proposed MBS item for LVAD implantation would be restricted to once per lifetime, MSAC also supported the amendment of existing MBS item 38621 to include wording allowing for LVAD replacement.

Consumer summary

This is an application from Abbott Medical Australia Pty Ltd requesting Medicare Benefits Schedule (MBS) listing of insertion of durable left ventricular assist device (LVAD) for use as destination therapy in patients with refractory heart failure.

Heart failure is a chronic progressive condition where the ability of the heart to pump blood around the body is impaired. This can be caused by various diseases or conditions such as a heart attack. There are several stages of heart failure. Refractory heart failure, also known as end-stage or advanced heart failure, is where the patient experiences persistent and progressive worsening in their heart function and symptoms despite receiving optimised medical treatment, which mainly includes medicines. These patients often require frequent hospitalisation and have poor survival if they do not receive further specialised advanced treatments, such as a heart transplant. However, some patients with refractory heart failure cannot have a heart transplant for various reasons.

An LVAD is a battery-operated mechanical pump that can help pump the patient's blood from the heart to the body. A surgeon would insert the LVAD into the left lower heart chamber, called the left ventricle. Some patients may temporarily receive an LVAD while they are waiting for a heart transplant. However, this application is seeking public funding to insert an LVAD in patients with refractory heart failure who cannot have a heart transplant. For these patients, LVAD would be used as a permanent treatment and is called destination therapy.

MSAC had previously considered this application at its meeting in April 2024. At that time MSAC had concluded that LVAD was more effective than the current standard of care for these patients but had asked for more information from the applicant in order to make a well-informed decision. MSAC requested further information from the applicant regarding aftercare services that would be accessed by patients after LVAD implantation, including the costs of these services. In the current resubmission the applicant provided the requested information by consulting with experts in Australian healthcare centres (including the centres that undertake LVAD implantation). Based on input from these experts, MSAC noted that aftercare services can be provided in person or in some instances through telehealth, and that the costs of these services are reasonable. With the updated information, MSAC concluded that LVAD for destination therapy is effective and good value for money for the patient population proposed in the application who currently have a very poor prognosis with no other effective treatment options.

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

MSAC supported the MBS listing for the insertion of a durable LVAD for destination therapy in the management of patients with refractory heart failure who are not eligible for a heart transplant. MSAC considered the proposed intervention to be more effective than the current standard of care (optimal medical management) for the target patient population, who have no other treatment alternatives. MSAC considered that LVAD for destination therapy would address a clinical need in this well-defined patient population with poor prognosis and accepted that LVAD for destination therapy was good value for money.

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

MSAC noted that this was a resubmission for MBS listing of insertion of durable LVAD for use as DT in patients with refractory heart failure despite OMM who are ineligible for cardiac transplantation. MSAC recalled that at its April 2024 meeting, MSAC considered and deferred its advice on public funding for LVAD for DT. MSAC recalled that the application had a well-defined patient population, who have a high unmet clinical need, due to having a very poor prognosis and no available effective treatment alternatives. Based on available indirect evidence presented in

the original submission, MSAC considered that use of a LVAD had superior effectiveness compared to OMM. At the time, MSAC deferred its advice on public funding due to uncertainties in the economic and financial analysis and requested the applicant:

- undertake consultation with Australian healthcare centres to obtain a more contemporary and informed estimate on the aftercare costs, (broken down by payer) and the format of aftercare services (e.g. in-person, telehealth and/or hybrid) following LVAD implantation in Australia
- describe how private patient funding for aftercare will be addressed by the public hospitals (the only sites where this service is currently available)
- re-specify the base case to use a time horizon of 10 years; apply OMM disease related costs in the 1st cycle of $0; apply a utility value of 0.64 for the 1st cycle in both the OMM and the LVAD arms, and in subsequent cycles of the OMM arm, and a utility value of 0.79 in the subsequent cycles of the LVAD arm; and further revise this base case to incorporate device replacement costs (other than for pump thrombosis) and aftercare costs informed by the above consultation with Australian hospitals
- update the financial analysis to incorporate the updated additional costs (as above) associated with the proposed service
- provide a proposed MBS item descriptor for the re-implantation of an LVAD for DT.

The applicant was granted a hearing, during which the applicant representatives presented information relating to aftercare services provided to patients implanted with LVAD. The applicant representatives noted that post-implantation patients require specialist care once a month, with the majority of these provided in person. It was noted that once stable, patients are also able to access this service through telehealth and provide the specialist with relevant information from their device. The representatives further noted that the number of additional general practitioner (GP) visits are likely to be low, as the patients are equipped to monitor anticoagulation through international normalised ratio (INR) testing and blood pressure monitoring at home. It was also noted that the specialist takes responsibility for anticoagulation management and driveline maintenance. It was noted that the newer LVAD, HeartMate 3, has more simplified aftercare compared to the older HeartWare pump due to the reduced number of complications associated with the newer LVAD model which would contribute to lower aftercare costs. The applicant representatives noted that there are no significant allied health costs related to post-discharge care, and patients are encouraged to attend a local rehabilitation clinic to improve exercise capacity and general fitness, as is done for all patients after a cardiac procedure.

MSAC noted the resubmission presented two economic analyses. MSAC considered the analysis referred to by the applicant as the 'likely overestimated base case' aligned most closely with the model specifications MSAC had previously advised and considered this to be the more appropriate analysis. MSAC noted that this analysis reduced the time horizon to 10 years, updated the utility values to align with MSAC's advice, increased the annual device replacement rate in Years 2+ from 1.1% to 2.2%, reduced the OMM disease related costs in the first cycle to $0, and updated the aftercare costs in Years 0-2 to $39,130.03/year. MSAC noted that the revised aftercare costs in the resubmission were informed by applicant conducted consultations with clinicians from all four adult heart transplant centres and one non-transplant centre. MSAC noted from the consultation input that the upper limit of aftercare costs per year following LVAD implantation is approximately $39,130.03. MSAC noted that this upper limit of aftercare costs does not include post-implantation rehabilitation costs, however considered that there are no reliable data sources to inform these costs and in addition considered from the applicant's hearing that these rehabilitation costs are unlikely to be substantial. MSAC noted that the revised economic model resulted in an ICER of $**redacted** per quality-adjusted life year (QALY) gained (corrected in the applicant's pre-MSAC response to $**redacted**), compared with $**redacted** per

QALY gained in the original submission. Although the ICER was high, MSAC considered it to be acceptable for the well-defined patient population who currently have a poor prognosis and a lack of effective alternative treatments.

MSAC noted from the applicant's hearing that the option of telehealth capability for aftercare would likely improve access and equity, particularly for rural and remote patients. MSAC also considered that technological improvements in LVADs (resulting in reduced complication rates) and changes in the model of patient care (where the patient is able to remote monitor/self-manage and thus requires fewer GP visits) have likely brought down aftercare costs in recent years.

MSAC noted the updated financial impact, including a cost to the MBS of $redacted to $redacted per year over 6 years, and an estimated cost to private health insurers of $redacted- $redacted per year over 6 years. This financial impact was based on the estimate that 20-22 LVAD procedures will be reimbursed on the MBS for DT per year. MSAC noted that although the 'likely overestimated base case' (the economic model presented in the resubmission which MSAC considered appropriate) included the upper limit of aftercare costs and an increased rate of LVAD replacement, these were not reflected in the budget impact analysis. MSAC noted that the updated financial impact did not include LVAD replacement costs for reasons other than pump thrombosis but considered that this would have a small impact on total budget implications, even at an increased rate of replacement at 2.2% as per the revised economic model. MSAC also noted that the financial analyses did not include post-implantation rehabilitation costs, consequently, the costs to the health system of adopting LVAD implantation as DT may be higher than estimated in the application. However, based on the information provided at the applicant's hearing, MSAC considered that post-discharge rehabilitation costs are unlikely to have a significant effect on the total financial impact.

Overall, MSAC accepted that LVAD for DT was cost-effective based on the total LVAD system price of $redacted which includes the LVAD implant kit, patient support kit bundle and the HeartMate 3 Mini.Apical cuff kit.

MSAC supported the MBS item descriptor in Table 1 for the initial LVAD implantation, in alignment with the advice provided by MSAC on the original application. For the initial implantation item, MSAC confirmed the proposed wording, including limiting the item to once per lifetime. In its previous consideration, MSAC considered restrictions based on frailty unwarranted as eligible patients would have already been rejected for a heart transplant due to frailty, and frail patients are likely to benefit most from the insertion of an LVAD due to the consequent increase in their cardiac output (MSAC 1749 PSD). In alignment with this, post-MSAC the committee agreed with the removal of the reference to 'frailty' and additional updates to section (b) of the explanatory note of the item descriptor as proposed by the Department. In its initial consideration, MSAC requested the applicant to propose an MBS item for re-implantation of an LVAD for DT. MSAC noted that an MBS item for re-implantation was not proposed in the resubmission as the applicant argued that re-implantation would be exceedingly rare based on the input provided by experts in the four adult transplant centres and one non-implanter centre. However, given that there is a restriction of once per lifetime in the proposed initial LVAD implant item (Table 1), MSAC considered that a separate MBS item for device replacement would be needed. For this purpose, MSAC supported the Department's proposal to amend existing MBS item for device removal, with no changes to the current fee (item 38621; Table 2).

Table 1: MSAC supported MBS item for initial LVAD implantation

Category 3 – Therapeutic Procedures
GroupT8 - Surgical Operations **Subgroup** 6 - Cardio-Thoracic **Subheading** 12 - Circulatory Support Procedures MBS item xxxx Insertion of a durable left ventricular assist device (LVAD) capable of providing mechanical circulatory support for at least six months, in an LVAD Patient for use as: (a) destination therapy in the management of a patient with refractory heart failure, despite optimal medical management including device use where appropriate, with INTERMACS profile 1–4, who is not eligible for cardiac transplantation; and (b) other than a service associated with a service to which item 11704, 11705, 11707, 11714, 18260, 33824, 38816, 38828 or 45503 applies. (H) Includes all associated intra-operative imaging. Multiple Operation Rule (Anaes.) (Assist.) Applicable only once per lifetime. Fee: $1,745.25 Benefit: 75% = $1,308.95 (See para TN.8.xx of explanatory notes to this Category)
Explanatory Note TN.8.xx Item xxxx must be performed using open exposure or minimally invasive surgery which excludes percutaneous and transcatheter techniques unless otherwise stated in the item. LVAD Patient An LVAD Patient means a patient who, as a result of an LVAD Case Conference, has been assessed as suitable for LVAD based on the following: (a) destination therapy in the management of a patient with refractory heart failure, despite optimal medical management including device use where appropriate, with INTERMACS profile 1–4, who is not eligible for cardiac transplantation. An LVAD Case Conference is a process by which: (a) there is a team of 4 or more participants, where: (i) the first participant is a cardiothoracic surgeon (ii) the second participant is an intensive care specialist or consultant physician who does not perform a service described in item xxxx for the patient being assessed; and (iii) the third participant is a transplant cardiologist who does not perform a service described in item xxxx for the patient being assessed; and (iv) the fourth participant is a transplant coordinator or LVAD coordinator; and (v) the first participant will perform the LVAD procedure (b) to receive the service described in item xxxx, the team should assess the following: (i) the patient's risk and technical suitability for a ventricular assist device implantation; and (ii) factors which limit life expectancy at the onset, such as ongoing malignancy or irreversible end-organ failure; and (iii) the patient's cognitive and psychosocial functioning is adequate, and (c) the result of the assessment is that the team makes a recommendation about whether or not the patient is suitable to receive the service described in item xxxx; and

Category 3 – Therapeutic Procedures
(d) the particulars of the assessment and recommendation are recorded in writing.

Table 2: MSAC supported the amendment of MBS item 38621 for device replacement (amendment denoted in blue text)

Category 3 – Therapeutic Procedures	
38621	**Group** T8 - Surgical Operations **Subgroup** 6 - Cardio-Thoracic **Subheading** 12 - Circulatory Support Procedures
Left or right ventricular assist device, removal or replacement of, as an independent procedure, other than a service associated with a service to which item 11704, 11705, 11707, 11714, 18260, 33824, 38627, 38816, 38828 or 45503 applies (H) Multiple Operation Rule (Anaes.) (Assist.) Fee: $868.45 Benefit: 75% = $651.35 (See para TN.8.67 of explanatory notes to this Category)	

4. Background

The Medical Services Advisory Committee (MSAC), at their meeting in April 2024, deferred its advice for public funding of insertion of durable LVAD for use as DT for patients with refractory heart failure, despite OMM, with an INTERMACS profile between 1-4 and who are not eligible for cardiac transplantation. MSAC considered that the clinical claim of superior efficacy and inferior safety of LVAD compared to the OMM made in the original applicant developed assessment report (ADAR) (MSAC Application 1749) was reasonable. However, MSAC considered that the magnitude of these effects was uncertain due to limitations in the available evidence. Furthermore, MSAC noted that the aftercare costs following LVAD implantation had not been adequately captured in the economic and financial analyses and considered that the resultant incremental cost-effectiveness ratio (ICER) and the financial impact may potentially be underestimated.

MSAC requested the applicant to consult Australian healthcare centres to obtain a more contemporary estimate of the aftercare costs following LVAD implantation in Australia. Furthermore, MSAC advised the applicant to revise the economic and financial analyses to incorporate the updated additional costs (particularly aftercare costs) associated with the LVAD implantation. MSAC considered that the resubmission could proceed via the direct MSAC assessment pathway.

Insertion of ventricular assist devices in patients with refractory heart failure is listed on the MBS for other populations, including MBS item 38615 (insertion of a left or right device) and MBS item 38618 (insertion of a left and right device) for use as bridge to transplant (BTT), bridge to candidacy (BTC), support for failure to wean from cardiopulmonary transplantation or support for acute cardiac failure <6 weeks. These items have been listed on the MBS since 1 November 1992, as per the MBS website for items 38615 and 38618.

Table 1 summarises the key matters of concern raised by MSAC in its consideration of the original submission ADAR (MSAC Application 1749).

Table 3 Summary of key matters of concern and the Commentary's view on how these were addressed

Component	Matter of concern	Commentary's view on how the current assessment report addresses it
MBS item for LVAD implantation	MSAC considered restrictions based on frailty unwarranted because eligible patients would be rejected for a heart transplant due to frailty (p3, MSAC 1749 PSD, April 2024 meeting).	Not addressed No amendments were made to the MBS item descriptor (p17, 1749 resubmission ADAR).
	MSAC considered that the proposed MBS item fee should include all intra-operative imaging required during implantation (p3, MSAC 1749 PSD, April 2024 meeting).	Addressed. The proposed MBS item descriptor states that the proposed fee included all associated intra-operative imaging.
	MSAC considered it unnecessary to specify that the LVAD should only be inserted into the left ventricle of the heart, given minimal evidence on the insertion into the right ventricle (p3, MSAC 1749 PSD, April 2024 meeting).	Addressed. The proposed MBS items align with MSAC advice.
MBS item for LVAD re-implantation	MSAC considered the MBS item for the initial insertion of LVAD should be restricted to once per lifetime, with a separate MBS item created and designated for re-implantation (p3, MSAC 1749 PSD, April 2024 meeting).	Not addressed. The resubmission did not propose an MBS item for re-implantation. It argued that that such an item is not necessary, given that re-implantation is extremely rare. This is based on the feedback from experts in four adult ventricular assist device implant centres in Australia.
Economic evaluation		
Time horizon	MSAC agreed with ESC that a time horizon of 40 years with a baseline age of 65 years is unreasonable as it extends beyond the average life expectancy and considered a time horizon of 10 years more appropriate (p4, MSAC 1749 PSD, April 2024 meeting).	Not adequately addressed in the "revised base case". The resubmission ADAR proposed 15 years as the time horizon for the "revised base case". The resubmission ADAR included 10-year time horizon, as per MSAC advice in the "likely overestimated case".
Utility value	MSAC agreed with ESC that utility values should be from the same source. MSAC considered that using utility values from Sato et al., 2022 of 0.64 (OMM all cycles; LVAD first cycle) and 0.79 (all other LVAD cycles) would have been more appropriate.	Addressed. Utility values were changed to be consistent with MSAC advice.

Component	Matter of concern	Commentary's view on how the current assessment report addresses it
Device replacement rate	MSAC noted that the ADAR model applied a 1% annual risk of pump thrombosis resulting in replacement from year 2 onwards. MSAC agreed with ESC and considered that device replacement for other reasons within the proposed 10-year time horizon should be considered.	Not adequately addressed in the "revised base case". The applicant doubled the device replacement rate to 2.2% from year 2 onwards in the sensitivity analysis (in the "likely overestimated case"), to address MSAC uncertainty but acknowledged the rate was not consistent with the evidence provided as MOMENTUM 3 trial reported no device replacement in the HM3 group in a 5-year follow-up, and a Western Australian study published by Silbert et al 2023[1] found no device replacement among DT patients implanted with LVAD devices.
Aftercare costs	MSAC raised concerns whether aftercare costs post LVAD implantation had been adequately captured in the economic analysis. This was based on anecdotal information that aftercare costs were possibly up to $ 1 million per LVAD patient in the first year after implantation. Therefore, MSAC considered that the ICER may potentially be underestimated and requested further information on additional costs of the service (especially aftercare costs) to be sourced from Australian hospitals that provide LVAD insertion for other indications, as well as secondary and tertiary healthcare centres that may be involved in patient post-management, to better inform the economic assessment.	Not adequately addressed. The resubmission ADAR did not present contemporary and informed aftercare costs (e.g. rehabilitation services by nursing and allied health staff) following LVAD implantation in Australia. Instead, the resubmission ADAR validated the costs proposed in the original ADAR through consultation with clinical experts in Australia. The consultation included interviews and a survey which sought feedback on the expected magnitude of aftercare costs, namely the health care costs following the LVAD index hospitalisation, in a DT population treated with the HM3 device (refer to MSAC Application 1749 Resubmission ADAR Attachment 2). Overall, the results of the survey support the magnitude of LVAD aftercare costs applied in the original submission ADAR ($**redacted** Year 1) which is approximately between Prichard et al., 2020 and Marasco et al., 2016 ($11,669.22 to $39,130.03). Of note, Prichard et al., 2020 and Marasco et al., 2016 reported LVAD aftercare costs in BTT/BTC patients implanted with older generation devices. The applicant maintained the aftercare costs as per original submission ADAR for the "revised base case" (Annual cost: Months 0-24 $**redacted**; Months 25+ $**redacted**. Additionally, the applicant proposed a "likely overestimated case" by applying aftercare costs from Prichard et al., 2020 (Annual cost: $39,130.03, inflated to 2024 index) in the first year.
	MSAC requested for a contemporary and informed estimate on the aftercare costs (broken down by payer) and the format of aftercare services (e.g. in-person, telehealth and/or hybrid) following LVAD implantation in Australia (p6, MSAC 1749 PSD, April 2024 meeting).	Not adequately addressed. Relevant payer distribution was partially addressed in Table 10 of the resubmission ADAR. The resubmission did not provide a breakdown of aftercare costs by payer and format (e.g., in-person or telehealth). It argued, based on experts' input, that the format of aftercare services should not matter, and the cost for these visits are included in the aftercare costs.

[1] Silbert B, Shah A, Dembo L, Hayes H, Larbalesteir R, Baumwol J. Left ventricular assist devices for treatment of refractory advanced heart failure: the Western Australian experience. Internal Medicine Journal (2023) 1–8

Component	Matter of concern	Commentary's view on how the current assessment report addresses it
	MSAC suggested that consultation should be undertaken to describe how private patient funding will be addressed (for aftercare) by the public hospitals (p6, MSAC 1749 PSD, April 2024 meeting).	Not addressed.
Revision to base case	MSAC requested to re-specify the base case to use a time horizon of 10 years, apply OMM disease related costs in the 1st cycle of $0, apply a utility value of 0.64 for the 1st cycle in both the OMM and the LVAD arms and in subsequent cycles of the OMM arm, and a utility value of 0.79 in the subsequent cycles of the LVAD arm, and further revise this base case to incorporate device replacement costs (other than for pump thrombosis) and aftercare costs informed by the above consultation with Australian hospitals (p6, MSAC 1749 PSD, April 2024 meeting).	Not adequately addressed. A "revised base case" was proposed in the resubmission ADAR, but the inputs were largely not aligned with MSAC's requests given that a 15-year time horizon (instead of 10 years requested by MSAC) and first year disease related cost in OMM arm of $4,862.80 (instead of $0 requested by MSAC) were applied. Furthermore, no changes were made on the device replacement rate and aftercare costs, from the original submission ADAR. A "likely overestimated case" was proposed in the resubmission ADAR with the incorporation of MSAC's request. However, there is still uncertainty in the aftercare costs.
Financial analysis	MSAC requested for update in the financial analysis to incorporate the updated additional costs associated with the proposed service (p6, MSAC 1749 PSD, April 2024 meeting).	Not adequately addressed. Device and disease related costs resulting in hospitalisation were presented in the resubmission ADAR but the costs did not incorporate revised risk and cost of pump replacement due to reasons other than pump thrombosis, or rehabilitation services within the aftercare costs.

Source: Table 1, p9-11 of MSAC Application 1749 Resubmission ADAR; MSAC 1749 PSD.
ADAR = applicant developed assessment report; BTT = bridge to transplant; BTC = bridge to candidacy; DT = destination therapy; ESC = Evaluation Sub-Committee; HM2 = HeartMate 2; HM3 = HeartMate 3; ICER = incremental cost-effectiveness ratio; LVAD = left ventricular assist device; MSAC = Medical Services Advisory Committee; OMM = optimal medical management; PSD = Public Summary Document.

5. Prerequisites to implementation of any funding advice

In the original submission ADAR (MSAC Application 1749), MSAC noted that the HeartMate 3 (HM3) is the most recent and current generation left ventricular assist device (LVAD) available in Australia. It is a third generation, fully magnetically levitated centrifugal flow ventricular assist device, listed on the Australian Register of Therapeutic Goods (ARTG) and the Prescribed List of Medical Devices and Human Tissue Products (PL) (MSAC 1749 Public Summary Document [PSD], pg2).

The indication for the HM3 LVAD as per the ARTG entry (ARTG ID: 300895) is:

- "The HeartMate 3 Left Ventricular Assist System is intended to provide long term hemodynamic support in patients with advanced, refractory left ventricular heart failure. It is intended either for temporary support, such as a bridge to cardiac transplantation (BTT), or as permanent destination therapy (DT). The HeartMate 3 is intended for use inside or outside the hospital".

On February 19, 2024, the U.S Food and Drugs Authority (FDA) reported Class I recall (i.e., the most serious type of recall which denotes the use of these devices may cause serious injuries or death) for HeartMate 2 (HM2) and HM3 by the Abbott/Thoratec Corp.[2] Of note, this recall was initiated by the company, and it was for the correction of affected devices and not a product removal. The reason for recalling was due to an Extrinsic Outflow Graft Obstruction (EOGO), which refers to development of biological material between the HeartMate Outflow Graft and the Outflow Graft Bend relief or additional components added during surgery. The EOGO can obstruct the device and reduce the device's ability to help the heart properly. There were 273 injuries, and 14 deaths associated with this issue.

6. Proposal for public funding

The resubmission ADAR presented a new proposed MBS item for the insertion of durable LVAD for DT. The MBS item proposed in the resubmission ADAR was identical to that in the 1749 PSD, apart from the update to the fee to $1,745.25 to be in line with the scheduled fee update for MBS item 38615 (insertion of left or right ventricular assist device) on 1 July 2024. The proposed fee includes all intra-operative imaging required during implantation as recommended by the MSAC. The item descriptor was device agnostic. However, it was noted that the HM3 is the only LVAD indicated for DT currently included on the ARTG (300895).

The proposed new MBS item descriptors for durable LVAD for DT including recommendations based on the Evaluation Sub Committee (ESC) and MSAC advice of previous submission (MSAC Application 1749) is provided in Table 2.

[2] U.S. Food and Drug Administration. Abbott/Thoratec Corp. Recalls HeartMate II and HeartMate 3 Left Ventricular Assist System (LVAS) due to Long-term Buildup Causing an Obstruction Abbott/Thoratec Corp. Recalls HeartMate II and HeartMate 3 Left Ventricular Assist System (LVAS) due to Long-term Buildup Causing an Obstruction | FDA (2024, accessed 18 Sep, 2024).

Table 4: Proposed new MBS item descriptors for durable LVAD for DT including edits based on ESC and MSAC advice on original submission (MSAC Application 1749)

Category 3 – Therapeutic Procedures
MBS item XXXX Insertion of a durable left ventricular assist device (LVAD) capable of providing mechanical circulatory support for at least six months, in an LVAD Patient for use as: (a) destination therapy in the management of a patient with refractory heart failure, despite optimal medical management including device use where appropriate, with INTERMACS profile 1–4, who is not eligible for cardiac transplantation; and (b) other than a service associated with a service to which item 11704, 11705, 11707, 11714, 18260, 33824, 38816, 38828 or 45503 applies. (H) Includes all associated intra-operative imaging. Multiple Operation Rule (Anaes.) (Assist.) Once per lifetime Fee: $1,745.25 Benefit: 75% = $1,308.95 (See para TN.8.xx of explanatory notes to this Category)
Explanatory Note TN.8.xx Item xxxx must be performed using open exposure or minimally invasive surgery which excludes percutaneous and transcatheter techniques unless otherwise stated in the item. LVAD Patient An LVAD Patient means a patient who, as a result of an LVAD Case Conference, has been assessed as suitable for LVAD based on the following: (a) destination therapy in the management of a patient with refractory heart failure, despite optimal medical management including device use where appropriate, with INTERMACS profile 1–4, who is not eligible for cardiac transplantation. An LVAD Case Conference is a process by which: a) there is a team of 4 or more participants, where: (i) the first participant is a cardiothoracic surgeon (ii) the second participant is an intensive care specialist or consultant physician who does not perform a service described in item xxxx for the patient being assessed; and (iii) the third participant is a transplant cardiologist who does not perform a service described in item xxxx for the patient being assessed; and (iv) the fourth participant is a transplant coordinator or LVAD coordinator; and (v) the first participant will perform the LVAD procedure (b) the team assesses a patient's risk and technical suitability to receive the service described in item xxxx, taking into account matters such as: (i) the patient's risk and technical suitability for a ventricular assist device implantation; and (ii) the patient's cognitive function ~~and frailty;~~ and (c) the result of the assessment is that the team makes a recommendation about whether or not the patient is suitable to receive the service described in item xxxx; and (d) the particulars of the assessment and recommendation are recorded in writing.

Source: Table 6, p18 of the MSAC Application 1749 Resubmission ADAR.
DT = Destination therapy; ESC = Evaluation subcommittee; INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support; LVAD = left ventricular assist device; MBS = Medicare Benefits Schedule; MSAC = Medical Services Advisory Committee; TN = technical notes
Notes: Yellow highlight indicates text added by the assessment group based on the MSAC advice on original submission. Strikethrough text indicates text deletions suggested by the assessment group based on the MSAC advice on original submission.

At the April 2024 Meeting, MSAC considered that the MBS item for the initial insertion of LVAD should be restricted to once per lifetime and requested the applicant to provide a proposed MBS item descriptor for the re-implantation of an LVAD for DT. However, the proposed MBS item descriptor in the resubmission ADAR did not restrict implantation to once per lifetime. The resubmission ADAR also argued that the incidence of device replacement was very low in recent devices based on evidence from MOMENTUM 3 Extended Follow-up Study[2] and Silbert et al., 2023[3], and therefore, it did not propose a separate MBS item for LVAD re-implantation. The resubmission ADAR noted that the MOMENTUM 3 Extended Follow-up Study[3] reported 10 confirmed device malfunctions with one resulting in a transplant after driveline repair in the HM3 cohort and no incidents of device replacement over 5-years of follow-up. Also, Silbert et al., 2023[4] study did not report any incidents of device replacement among all eight DT patients. Of note, this cohort included the two longest surviving DT patients worldwide (11.3 and 10.5 years, both now deceased).

The resubmission ADAR claimed that the consultation feedback from experts in the four adult LVAD implant centres in Australia were supportive of not having a separate MBS item for the re-implantation of LVAD for DT, given the need for reimplantation would be exceedingly rare and quoted from the clinicians survey "The very vast majority of DT patients will not be suitable for a redo LVAD and would under those circumstances follow a palliative pathway" (MSAC Application 1749 Resubmission ADAR Attachment 2) to support the claim. However, the commentary noted that the survey of clinicians was focused on aftercare costs. The commentary could not identify the details or quotes relevant to the device replacement in Attachment 2 of the MSAC Application 1749 Resubmission ADAR.

The commentary considered that the incidence of device replacement provided in the resubmission ADAR was underestimated (refer to Section 10: Incidence of device replacement). The resubmission ADAR considered pump thrombosis as the only reason for device replacement whereas device malfunction and infection could be other possible indications for device replacement.[5] Therefore, there will be a cohort of patients in the proposed population who would require device replacement and an MBS item for the re-implantation of an LVAD for DT will be required as the proposed MBS item descriptor restricts implantation for once per lifetime.

Of note, there are three MBS items currently available relevant for the removal of, adjustment of, or repositioning of LVAD;

- MBS item 38621: Left or right ventricular assist device, removal of, as an independent procedure, other than a service associated with a service to which item 11704, 11705, 11707, 11714, 18260, 33824, 38627, 38816, 38828 or 45503 applies (H).
- MBS item 38624: Left and right ventricular assist device, removal of, as an independent procedure, other than a service associated with a service to which item 11704, 11705, 11707, 11714, 18260, 33824, 38627, 38816, 38828 or 45503 applies (H)
- MBS item 38627: Extra-corporeal membrane oxygenation, bypass or ventricular assist device cannulae, adjustment and re-positioning of, by open operation, in patients supported by these devices, other than a service associated with a service to which item 11704, 11705, 11707, 11714, 18260, 33824, 38627, 38816, 38828 or 45503 applies

[3] MOMENTUM 3 Pivotal Cohort Extended Follow-Up Post-Approval Study CSR

[4] Silbert B, Shah A, Dembo L, Hayes H, Larbalestier R, Baumwol J. Left ventricular assist devices for treatment of refractory advanced heart failure: the Western Australian experience. Internal Medicine Journal (2023) 1–8

[5] Jimenez-Contreras F, Rames JD, Schroder J et al. Long-term predictors of morbidity and mortality in patients following LVAD replacement. Artif Organs. 2024 Feb;48(2):157-165. doi: 10.1111/aor.14651.

MSAC advice was sought whether the new descriptor for re-implantation of LVAD for DT should refer to the above items.

7. Population

The proposed population in the original submission ADAR was patients with advanced HF despite OMM, with INTERMACS profile 1–4, who are not eligible for cardiac transplantation and in whom an LVAD is used as DT (i.e., final therapy). The resubmission ADAR did not suggest any changes to the proposed population.

MSAC noted that the prognosis for this population to be very poor and there was a high clinical need for the proposed patient population who are on OMM with no other treatment alternatives, as determined by a multidisciplinary team (MSAC 1749 PSD, pg3).

8. Comparator

The OMM, which is also referred to as guideline directed medical therapy (GDMT) or optimal medical therapy (OMT), was the proposed comparator to insertion of an LVAD as DT. The OMM can include quadruple pharmacological treatments with renin-angiotensin-system inhibitors, beta blockers, mineralocorticoid receptor antagonists and sodium glucose cotransporter 2 (SGLT2) inhibitors; and non-pharmacological interventions such as pacing, angioplasty, hemofiltration and ventilation. The comparator is consistent with the original submission ADAR.

9. Summary of public consultation input

Refer to the April 2024 PSD on the MSAC website.

10. Characteristics of the evidence base

The resubmission ADAR did not present any new clinical evidence comparing HM3 with OMM other than the evidence provided in the original submission ADAR. MSAC noted that the clinical evidence for the original submission ADAR was based on indirect treatment comparisons (ITC) derived from three randomised controlled trials (RCTs; MOMENTUM3[6] , Slaughter et al., 2009[7] , REMATCH[8]) and one observational study (ROADMAP)[9] .

- Two-step Bucher ITC (REMATCH): an ITC of HM3 versus OMM constructed via HM2 and HM XVE (via Slaughter et al., 2009; REMATCH and MOMENTUM 3).
- One-step Bucher ITC (ROADMAP): an ITC of HM3 versus OMM constructed via HM2 (based on MOMENTUM 3 and the ROADMAP observational study).

[6] Mehra MR, Uriel N, Naka Y, et al. A Fully Magnetically Levitated Left Ventricular Assist Device - Final Report. N Engl J Med 2019; 380: 1618-1627. 20190317. DOI: 10.1056/NEJMoa1900486.

[7] Slaughter MS, Rogers JG, Milano CA, et al. Advanced heart failure treated with continuous-flow left ventricular assist device. N Engl J Med 2009; 361: 2241-2251. 20091117. DOI: 10.1056/NEJMoa0909938.

[8] Rose EA, Gelijns AC, Moskowitz AJ, et al. Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med 2001; 345: 1435-1443. DOI: 10.1056/NEJMoa012175.

[9] Estep JD, Starling RC, Horstmanshof DA, et al. Risk Assessment and Comparative Effectiveness of Left Ventricular Assist Device and Medical Management in Ambulatory Heart Failure Patients (ROADMAP). The Journal of Heart and Lung Transplantation 2015

- Naïve comparison: a naïve comparison of HM3 (from MOMENTUM 3, 98% of the patients were INTERMACS 1–4) versus OMM (primarily from REMATCH, suggestive of INTERMACS profiles 1–3).

At its April 2024 Meeting, MSAC noted that there were differences in study characteristics that affect the transitivity of the ITC including the intent of treatment (i.e., DT), INTERMACS scores, follow-up duration, and differences in the demographics of participants.

MSAC also noted two ongoing RCTs (SweVAD and AMBU-VAD), comparing efficacy and safety of HM3 and OMM, are in the recruitment phase. However, the resubmission ADAR stated that these two ongoing RCTs are still in the recruitment phase, hence no new data available at the time of writing this resubmission.

11. Comparative safety

The original submission ADAR presented all cause adverse events (all cause AEs) and serious adverse events (SAEs) as the main safety outcomes and the safety claim was mainly based on the two-step Bucher ITC of HM3 vs OMM (via HM2 and HM XVE).

At the April 2024 meeting, MSAC considered that the original submission ADAR safety claim, that the device has inferior safety compared to OMM, was reasonable. However, MSAC considered that the safety analysis was limited due to the indirect nature of the clinical evidence provided, the differences in the characteristics of the trials affect the transitivity of the studies in the ITC and the inconsistent/under-reporting of adverse events and hospitalisations in the trials (MSAC 1749 PSD, pg4).

12. Comparative effectiveness

Overall survival (OS) was the primary effectiveness outcome presented in the original submission ADAR. However, the definition of OS across the included trials were not consistent. OS data in the MOMENTUM 3 trial, REMATCH trial and Slaughter et al., 2009 trial was based on the actuarial survival (i.e., defined as all-cause mortality in as-treated population). In contrast, the OS data from ROADMAP was based on event-free survival of as-treated population, defined as patients received LVAD as DT free of urgent heart transplant or explant, and OMM patients free of LVAD or urgent heart transplant. The secondary outcomes (i.e., functional status [as assessed by NYHA classification and six minute walking test] and quality of life outcomes [as assessed by EQ-5D VAS]) was based on naïve indirect comparisons as data was not available to perform anchored ITCs.

At its April 2024 meeting, the MSAC considered that the original submission ADAR claim, superior effectiveness of LVAD compared to OMM, was reasonable. However, MSAC considered that the magnitude of this effect was uncertain due to absence of any direct evidence comparing HM3 and OMM, and the use of non-contemporaneous data from the REMATCH trial conducted prior to 2001 for the OMM arm. MSAC further considered that implantation of an HM3 resulted in improved functional status and quality of life outcomes, yet reiterated uncertainty surrounding the magnitude of the incremental effects due to the limitations in the available data. (MSAC 1749 PSD, pg4).

Clinical claim

The resubmission ADAR did not suggest any changes to the proposed clinical claim presented in the original submission ADAR. At its April 2024 meeting, the MSAC considered that the available

clinical evidence is associated with a high risk of bias leading to uncertainty in the magnitude of effect due to:

- absence of any direct comparisons between HM3 and OMM,
- data from the REMATCH trial being non-contemporary, and
- differences in study characteristics that affect the transitivity of the ITCs including differences in intent of treatment (i.e. DT), INTERMACS scores, demographics of participants and clinical endpoints.

13. Economic evaluation

The resubmission ADAR presented revisions to the cost-effectiveness analysis in response to MSAC advice at its April 2024 Meeting. Of note, a cost-utility analysis (CUA) was presented in the resubmission ADAR and therefore, for consistency, the commentary considered CUA as the economic evaluation. The resubmission considered CUA as appropriate economic evaluation approach based on the clinical claim of superior efficacy and inferior safety of HM3 LVAD + OMM, compared to OMM, as stated in the original submission ADAR. Most of the model inputs remained unchanged in the resubmission and a summary of the economic evaluation is presented in Table 3.

Table 5 Summary of the economic evaluation

Component	Description	Change or update in the current resubmission ADAR
Perspective	Australian Health care system perspective	*No change*
Population	Patients with advanced HF despite OMM, with INTERMACS profile 1–4, who are not eligible for cardiac transplantation and in whom LVAD is used as DT (i.e., final therapy)	*No change*
Comparator	OMM – also referred to as GDMT or OMT	*No change*
Type(s) of analysis	Cost-utility analysis	*No change*
Outcomes	Life years QALYs Healthcare resource costs	*No change*
Time horizon	Lifetime horizon (baseline age is 65) vs. 5-year in the key trial MOMENTUM 3.	*Revised base case: 15 years* *"Likely overestimated case": 10 years*
Computational method	Partitioned survival analysis	*No change*
Generation of the base case	Modelled economic evaluation: Trial based effectiveness outcomes based on naïve comparison are derived from subgroup analyses of MOMENTUM 3 (5-year OS data from the MOMENTUM 3 study for a DT subgroup excluding patients receiving heart transplant for the LVAD arm; INTERMACS 1-7)[a] and REMATCH (patients receiving LVAD as DT; INTERMACS suggestive of 1-3 for the OMM arm) in accordance with the target MBS population (in relation to the patients receiving LVAD as DT) in the submission Trial based OS curves are extrapolated over a lifetime horizon. Healthcare resource use and utility weights derived from the literature are applied to generate total costs and QALYs in each treatment arm.	*No change*
Health states	Alive and Dead	*No change*
Cycle length	1 month	*No change*
Transition probabilities	No specific transition probabilities are modelled. Health state allocation over time determined by OS curves from MOMENTUM 3 (LVAD arm) and REMATCH (OMM arm)	*No change*
Discount rate	5% for both costs and outcomes	*No change*
Software	Excel	*No change*

Source: Table 8, pp27-28 of the MSAC 1749 PSD.
DT = destination therapy; GDMT = Guideline directed medical therapy; HF = heart failure; ICER = incremental cost-effectiveness ratio; INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support; LVAD = left ventricular assist device; MBS = Medicare benefit schedule; OMM = optimal medical management; OMT = optimal medical therapy; OS = overall survival; QALY = quality adjusted life year.
Notes: [a] DT subgroup of MOMENTUM 3 included INTERMACS 1-3 83.8% and INTERMACS 4-7 16.1% in HM3 arm, and INTERMACS 1-3 85.2% and INTERMACS 4-7 14.8% in HM2 arm. No separate data available for the INTERMACS 1-4, the target population in this application.
Italics indicates addition during commentary.

In response to the MSAC's re-specification of the base case, the resubmission ADAR proposed two sets of revised modelling assumptions namely "revised base case" and "likely over estimated base case". The resubmission ADAR noted that the revised base case addresses MSAC advice

and considered that it aligns most closely with accurate estimates in the target MBS population. The resubmission ADAR noted that the "likely overestimated base case" is intended to reflect the combined impact of assumptions which are not necessarily consistent with current evidence or expert opinion but are conservative to the extent that it would reflect a 'worse case' scenario for the cost-effectiveness of LVAD in the Australian setting.

Table 4 provides a summary of the revisions to the economic analysis in the resubmission ADAR.

Table 6 Summary of revisions to the economic analysis in the resubmission ADAR.

MSAC advice	Approach in original submission ADAR	Change or update in the current resubmission ADAR	*Commentary Comments*
Time horizon: 10 years	Lifetime horizon (a time horizon of 40 years with a baseline age of 65 years)	"Revised base case": 15 years "Likely overestimated case": 10 years	*Changes were reasonable. However, time horizon was a key driver of the model and the ICER increased by 16% to $**redacted**/QALY when the time horizon was reduced from 15 to 10 years.* The resubmission ADAR considered that a 10-year time horizon likely underestimates the life expectancy of a proportion of patients. The resubmission ADAR justified that 4 out of 9 patients (*median age at implant was 71 years*) implanted with newer generation LVAD devices (HVAD, HM2 and HM3) with DT remained alive beyond ten years (years alive at time of publication ranged from 10.1 to 11.2 years), based on an abstract which reviewed the outcomes of DT patients in a Western Australian LVAD program (McLean J. et al 2024[a]).
Utility values: 0.64 (OMM all cycles; LVAD first cycle) and 0.79 (all other LVAD cycles) based on Sato et al., 2022	OMM arm First cycle = 0.44 Subsequent cycles = 0.44 LVAD arm First cycle = 0.44 Subsequent cycles = 0.79	OMM arm First cycle = 0.64 Subsequent cycles = 0.64 LVAD arm First cycle = 0.64 Subsequent cycles = 0.79	*Changes were consistent with MSAC advice.*
Incidence of device replacement To consider device replacement for other reasons within the proposed 10-year time horizon.	Annual risk of device replacement: Years 0-2 = 0.01 Years 2+ = 0.011	"Revised base case": Annual risk of device replacement: Years 0-2 = 0.01 Years 2+ = 0.011 "Likely overestimated case": Annual risk of device replacement:	*The "revised base case" in the resubmission ADAR did not change from the original submission ADAR.* *This is inappropriate because the resubmission ADAR assumed the risk of device replacement based on pump thrombosis only. Other potential reasons for device replacement include device*

		Years 0-2 = 0.01 Years 2+ = 0.022	*malfunction and infection. Based on the INTERMACS 2023 Annual Report by Jorde et al., 2024[b], the incidence of device malfunction/pump thrombosis (>90 days after implant) over a 5-year period, was 0.04 EPPY. Increasing the device replacement rate from 0.011 to 0.04 EPPY in year 2-5 would increase ICER of the "revised base case" by 11% to $**redacted**/QALY.* The resubmission ADAR stated there was no device replacement in the HM3 arm during the 5-year follow up of MOMENTUM 3 trial (Mehra et al., 2022[c]). *However, there was a high percentage of missing data of serious adverse events in that study due to COVID-19 pandemic.* *The resubmission ADAR increased the incidence of device replacement Years 2+ in the 'likely over estimated case'. The annual risk of device replacement of 0.022 EPPY (double the rate that was proposed in the original submission) was an assumption proposed in the resubmission ADAR to address MSAC uncertainty.*
<u>OMM disease related costs in the first cycle:</u> $0	First cycle costs = $34,218.02 (based on Prichard et al., 2020)	"Revised base case" = $4,958.11 (cost inflated to year 2024, based on Table 9 of MSAC Application 1749 Resubmission ADAR and Section 3 LVAD CEA Workbook) "Likely overestimated case" = $0	First cycle costs used in the "revised base case" were based on the pre-index admission phase of Prichard et al., 2020, *which was reasonable. However, ongoing management cost of $148.08 was also applied to both LVAD and OMM arms in the first cycle. Therefore, the first cycle costs in the "revised base case" was likely overestimated, though minimally.*
<u>Aftercare costs in LVAD patients</u> Additional costs of service, especially aftercare costs, to be sourced from Australian hospitals which provide LVAD insertion for other indications, as well as secondary and tertiary healthcare centres that may be	Annual cost: Months 0-24 $**redacted**; Months 25+ $**redacted** Aftercare costs in LVAD patients were divided into the following: • Ongoing monitoring: frequency of follow-up visits and testing based on guidelines and costed based on relevant MBS items	"Revised base case": Annual cost: Months 0-24 $**redacted**; Months 25+ $**redacted** "Likely overestimated case": Annual cost: $39,130.03 based on Prichard et al., 2020 inflated to 2024 index, in the first year.	*The "revised base case" in the resubmission ADAR did not change from the original submission ADAR. However, the applicant made changes to the aftercare costs in the 'likely over estimated case'.* *The resubmission ADAR did not address MSAC's request for a contemporary and informed estimate of the aftercare costs following LVAD implantation in Australia. Instead, the resubmission*

involved in patient post-management, to better inform the economic assessment	• Device and disease related costs: frequency of device and disease related complications including device replacement based on 5-year follow-up data from MOMENTUM 3 and costed based on corresponding AR-DRG costs • Ongoing therapeutic management and battery replacement: guideline directed treatment type and frequency costed based on PBS drug costs (DPMQ).		*proposed an aftercare cost of $39,130.03 based on Prichard et al., 2020 in the" likely overestimated case".*

Source: Table 7, p20-23; Table 19, p37; Table 9, p25 of MSAC Application 1749 Resubmission ADAR;
AR-DRG = Australian Refined Diagnosis Related Groups; CEA = cost effectiveness analysis; DPMQ = dispensed price for maximum quantity; DT = destination therapy; EPPY = event per patient per year; HM = HeartMate; HVAD = HeartWare ventricular assist device; INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support; LVAD = left ventricular assist device; MSAC = Medical Services Advisory Committee; OMM = optimal medical management; PBS = Pharmaceutical Benefits Scheme.
Notes: *Italics indicates viewpoint of the commentary*
[a] McLean J, Baumwol J, Shah A et al. Survival in End-Stage HF Patients Ineligible for Cardiac Transplant can Exceed 10 Years With LVAD 'Destination Therapy'. Heart, Lung and Circulation. 2024;33(4):s287. https://doi.org/10.1016/j.hlc.2024.06.350.
[b] Jorde UP, Saeed O, Koehl D et al. The Society of Thoracic Surgeons Intermacs 2023 Annual Report: Focus on Magnetically Levitated Devices. Ann Thorac Surg. 2024 Jan;117(1):33-44 10.1016/j.athoracsur.2023.11.004;
[c] Mehra MR, Goldstein DJ, Cleveland JC et al. Five-Year Outcomes in Patients With Fully Magnetically Levitated vs Axial-Flow Left Ventricular Assist Devices in the MOMENTUM 3 Randomized Trial. JAMA. 2022 Sep 27;328(12):1233-1242. doi: 10.1001/jama.2022.16197.

Time horizon

A lifetime horizon was proposed in the original submission ADAR. MSAC advised that a time horizon of 40 years with a baseline age of 65 years was unreasonable as it extends beyond the average life expectancy. MSAC considered a 10-year time horizon was more appropriate. In the resubmission ADAR, a "revised base case" with a time horizon of 15 years was presented. The resubmission ADAR disputed that a 10-year time horizon likely underestimated the life expectancy of a meaningful proportion of patients treated with LVAD as DT. McLean et al., 2024[10], an abstract which reviewed the outcomes of DT patients in the Western Australian LVAD program, reported four out of nine patients implanted with newer generation LVAD (HeartWare ventricular assist device (HVAD), HM2 and HM3) for DT remained alive beyond ten years (years alive at time of publication ranged from 10.1 to 11.2 years). Of note, the median age at implant was 71 years in the McLean et al., 2024. A 15-year time horizon may be reasonable as McLean et al., 2024 reported older patients, in contrast to baseline age of 65 years, in Australia who survived beyond 10 years post-LVAD implantation. However, time horizon was a key driver of the model and the ICER increased by 16% to $60,355/QALY when the time horizon was reduced from 15 to 10 years.

[10] McLean J, Bauwol J, Shah A et al. Survival in End-Stage HF Patients Ineligible for Cardiac Transplant can Exceed 10 Years With LVAD 'Destination Therapy'. [abstract] Heart, Lunch and Circulation 2024; 33(4):s287. https://doi.org/10.1016/j.hlc.2024.06.350

Health state utility values

In the original submission ADAR, the health state utility value for first cycle was 0.44 in both LVAD and OMM arms, based on Prichard et al., 2021[11]. In the subsequent cycles, the ADAR assumed constant utility (0.44) in OMM arm, and a utility of 0.79 in the LVAD arm, based on Sato et al., 2022[12]. MSAC commented that the utility values should be from the same source and considered the utility values from Sato et al., 2022 of 0.64 (OMM all cycles; LVAD first cycle) and 0.79 (all other LVAD cycles) would be more appropriate. In the resubmission ADAR, the utility values were changed and consistent with MSAC advice. However, the resubmission ADAR reasoned that a utility value of 0.64 in the OMM arm was likely overestimated as the OMM patients would mainly be in INTERMACS 1-3 and non-ambulatory with intravenous inotropic therapy in hospital. This claim was not supported by evidence. Based on two Australian studies, Kularatna S et al., 2017[13] reported a utility value of 0.67 in heart failure patients with NYHA class IV, and Maru S et al., 2016[14] estimated a mean utility score of 0.71 in heart failure patients with NYHA class II-IV. Of note, NYHA class IV includes INTERMACS profiles 1-5[15], which corresponds to the target population of this resubmission ADAR (INTERMACS profiles 1-4). The commentary considered that the use of a constant utility value of 0.64 in the OMM arm in all cycles to be conservative, considering advanced heart failure patients on OMM deteriorate over time.

Incidence of device replacement

In the original submission ADAR, the risk of pump thrombosis and hence device replacement was 0.010 events per patient per year (EPPY) in year 0-2, and 0.011 EPPY in year 2-5, based on MOMENTUM 3. The original submission ADAR considered the assumption of pump thrombosis resulting in device replacement conservative, hence the incidence of device replacement remained unchanged in the resubmission ADAR. Instead, an incidence rate of 0.022 EPPY in year 2 onwards was applied as a sensitivity analysis assumption in the 'likely overestimated case' in response to MSAC's concerns that a 1% annual risk of pump thrombosis leading to device replacement was underestimated in the proposed 10-year time horizon. The commentary considered that the proposed device replacement rate of 0.022 EPPY (year 2-5) in the resubmission ADAR was uncertain as it was not evidence-based. The device replacement rate in year 2-5 could potentially be higher based on the INTERMACS 2023 Annual Report[16]. Although INTERMACS 2023 Annual Report did not explicitly report the device replacement rate, it reported 0.04 EPPY for the rate of device malfunction/pump thrombosis, which are potential reasons for device replacement among other reasons (e.g. infection, mitral valve dysfunction) reported in

[11] Prichard RA, Zhao FL, Mcdonagh J, Goodall S, Davidson PM, Newton PJ, Farr-Wharton B, Hayward CS. Discrepancies between proxy estimates and patient reported, health related, quality of life: minding the gap between patient and clinician perceptions in heart failure. Qual Life Res. 2021 Apr;30(4):1049-1059. doi: 10.1007/s11136-020-02722-z.

[12] Sato T, Kobayashi Y, Nagai T et al. Long-term preservation of functional capacity and quality of life in advanced heart failure patients with bridge to transplant therapy: A report from Japanese nationwide multicenter registry. Int J Cardiol. 2022 Jun 1;356:66-72. https://doi.org/10.1016/j.ijcard.2022.03.044

[13] Kularatna S, Byrnes J, Chan YK et al. Comparison of contemporaneous responses for EQ-5D-3L and Minnesota Living with Heart Failure; a case for disease specific multiattribute utility instrument in cardiovascular conditions. International Journal of Cardiology 2017; 227:172-6. https://doi.org/10.1016/j.ijcard.2016.11.030

[14] Maru S, Byrnes JM, Carrington MJ et al. Long-term cost-effectiveness of home versus clinic-based management of chronic heart failure: the WHICH? study. Journal of Medical Economics 2016; 20(4):318-27. https://doi.org/10.1080/13696998.2016.1261031

[15] Truby, L, Rogers, J. Advanced Heart Failure: Epidemiology, Diagnosis, and Therapeutic Approaches. J Am Coll Cardiol HF 2020; 8 (7) 523–536. https://doi.org/10.1016/j.jchf.2020.01.014

[16] Jorde UP et al. The Society of Thoracic Surgeons Intermacs 2023 Annual Report: Focus on Magnetically Levitated Devices. Ann Thorac Surg. 2024 Jan;117(1):33-44. https://doi.org/10.1016/j.athoracsur.2023.11.004

Jimenez Contreras F et al., 2024[4] and Mehra et al., 2019[5]. Increasing the device replacement rate from 0.011 to 0.04 EPPY in year 2-5 would increase the ICER by 11% to $57,627/QALY.

Table 5 summarises the incidence of device malfunction, pump thrombosis and device related infection from MOMENTUM 3 trial and INTERMACS 2023 Annual Report.

Table 7 Incidence of suspected device malfunction/pump thrombosis/infection with HM3

Annual incidence of adverse event with HM3	**0-2 years (EPPY)**	**2-5 years (EPPY)**	**Population**
MOMENTUM 3[1,2]			
LVAS driveline infection	0.23	0.11[a]	Mean age 62 years; n=515; DT (62%); INTERMACS profiles 1-3 (85%)
Suspected or confirmed pump thrombosis	0.01	0.011[a]	
Device replacement	0.01	0[a]	
Annual incidence of adverse event with HM3	**≤90 days after implant;**	**>90 days after implant**	**Population**
INTERMACS 2023 Annual Report[3]			
Device malfunction/pump thrombus	0.06	0.04	Mean age 60 years; n=10,920; DT (73%); INTERMACS profiles 1-3 (86%)
Mechanical circulatory support-related infection	0.15	0.18	
Device replacement	NR	NR	

Source: Compiled for the commentary from 1. Mehra MR, Goldstein DJ, Cleveland JC et al. Five-Year Outcomes in Patients With Fully Magnetically Levitated vs Axial-Flow Left Ventricular Assist Devices in the MOMENTUM 3 Randomized Trial. JAMA 2022; https://doi.org/10.1001/jama.2022.16197 2. Mehra MR, Uriel N, Naka Y et al. A Fully Magnetically Levitated Left Ventricular Assist Device - Final Report. N Engl J Med. 2019 Apr 25;380(17):1618-1627. https://doi.org/10.1056/nejmoa1900486 3. Jorde UP et al. The Society of Thoracic Surgeons Intermacs 2023 Annual Report: Focus on Magnetically Levitated Devices. Ann Thorac Surg. 2024 Jan;117(1):33-44. https://doi.org/10.1016/j.athoracsur.2023.11.004

BTT = bridge to transplant; DT = destination therapy; EPPY = events per patient-year; HM3 = HeartMate 3; INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support; LVAS = left ventricular assist system; NR = not reported.

Notes: [a] Mehra et al, 2022 acknowledged that there was a high percentage of missing data (only 178 people included in the follow up in year 2-5, compared to 515 people in the pivotal cohort) in serious adverse events due to COVID -19 pandemic.

OMM disease related costs in the first cycle

The original submission ADAR presented the OMM disease related cost of $34,218.02 in the first cycle, based on the pre-implant period where patients are in critical care as reported by Prichard et al., 2020. MSAC suggested to re-specify the base case with OMM disease related costs of $0 in the first cycle. The resubmission considered a cost of $0 in the first cycle to be clinically invalid as patients in OMM arm have poor health and high mortality rate. The resubmission revised the OMM disease related first cycle cost based on the pre-index admission phase of Prichard et al., 2020 i.e. median per diem cost of pre-admission of $134.00, inflated to $162.89 (2024 price based on Australian Institute of Health and Welfare (AIHW) inflation index) and multiplied by 30.4375 days, which is the average number of days in a month, resulting in the first cycle cost in OMM arm to be $4,985.11 (Table 9 of MSAC Application 1749 Resubmission ADAR).

The commentary noted that in addition to the $4,985.11, an ongoing management cost of $148.08/month was included in both OMM and LVAD arms, resulting in an overestimated cost to the OMM arm, albeit minimally. The commentary considered the addition of $148.08 to OMM arm was double-counting because the sum of $4,985.11 had included the cost of medicine, outpatient care and imaging/pathology.

The resubmission ADAR presented a “likely overestimated case” with a first cycle OMM cost of $0.

Aftercare costs in LVAD patients

In the original submission ADAR, LVAD aftercare costs were calculated using a bottom up approach which incorporated the costs of ongoing monitoring, therapeutic management, battery replacement, device and disease related complications. Table 6 summarises the LVAD aftercare costs with the relevant payers in the "revised base case".

Table 8 LVAD aftercare costs by payer ("revised base case")

Component cost	Cost per year per patient in the original submission ADAR	Cost per year per patient in the resubmission ADAR	Relevant payer	*Comments*
Ongoing monitoring	$649.95	$676.45	MBS	*Costs were updated in the resubmission ADAR.* ECG once per year, MBS item 11713 (full fee *$79.45);* Clinic visit once per month, MBS item 105 (full fee *$49.75)*
Anticoagulation management: Medications (warfarin and aspirin)	$219.76	$225.10	PBS	*Costs were updated in the resubmission ADAR.* Warfarin (PBS item 2211J) costs $18.87 for 50 tablets. Aspirin (PBS item 4076M) costs $21.50 for 90 tablets
Anticoagulation management: INR testing	$414.00	$471.60	*MBS*	*Costs were updated in the resubmission ADAR.* MBS item 65120 ($13.70) and 74995 ($4.00) for 20 times per year; MBS item 3 ($19.60) for 6 times per year
Antihypertensive management	$392.71	$403.87	PBS	*Costs presented in the Section 3 LVAD CEA workbook were inaccurate as they were multiplied by 356.25 days. The total cost was updated to $414.07 in the commentary, by multiplying with 365.25 days.* Perindopril (PBS item 8704D) costs $17.84 for 30 tablets. Atenolol (PBS item 1081X) costs $16.17 for 30 tablets.
Battery replacement	$2,296.00 applied to alive LVAD patients every three years	$2,296.00	Private health funds	*No changes in the resubmission.* *The cost (item code SJ385) was reduced to $2,295, based on the August 2024 Prescribed List.*
Disease related complications	Months 0-24: $14,579.96 Months 25+: $3,114.68	Months 0-24: $14,579.96 Months 25+: $3,114.68	Private health funds *or public hospitals*	No changes from the original submission ADAR[a].

Device related adverse events	Months 0-24: $**redacted** Months 25+: $**redacted**	Months 0-24: $**redacted** Months 25+: $**redacted**	Private health funds or public hospitals	*The presented costs for the original submission ADAR were incorrect, whereby the calculated sums were $3,165.24 ($263.77[a] multiplied by 12) in months 0-24 and $2,948.28 ($245.69[a] multiplied by 12) in months 25+, based on commentary's calculation. Hence, the device related adverse event costs in the resubmission ADAR increased slightly from the original submission ADAR.* *Cost of device replacement due to reasons other than pump thrombosis was not included in the resubmission ADAR.*
Total	Months 0-24 $**redacted** Months 25+ $**redacted**	Months 0-24 $**redacted** Months 25+ $**redacted**	-	*The resubmission ADAR has calculated the total cost by sum of all the above component costs but have excluded battery replacement costs and noted that this was because this cost is only applied once every three years.* *The presented costs were incorrect. The total costs in the original submission ADAR were $19,421.62 (months 0-24) and $7,739.38 (months 25+), based on commentary's calculation. The total costs in the resubmission ADAR for the "revised base case" were $19,547.16 (months 0-24) and $7,866.39 (month 25+), based on commentary's calculation. Overall, the total costs used in the "revised base case" increased slightly from the original submission ADAR.*

Source: Table 10, p27; Table 19, p37 of the MSAC Application 1749 Resubmission ADAR; Section 3 LVAD CEA Workbook of MSAC Application 1749 Resubmission ADAR.
DPMQ = dispensed price for maximum quantity; ECG = electrocardiogram; INR = international normalised ratio; LVAD = left ventricular assist device; MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme.
Notes: Italics denote additions made by the Department or the assessment group.
[a] Costs were based on the MOMENTUM 3 trial. Costs obtained from Table 59, p214 of Attachment 1_MSAC Application 1749

The resubmission ADAR applied an alternative analysis in the "likely overestimated case" by assuming the aftercare costs in terms of disease and device related complications to be equal to Prichard et al., 2020 (adjusted to 2024 prices: $39,130.03) in year 0-2. In subsequent years LVAD aftercare costs were considered to be equal to the "revised base case" ($**redacted**). Of note, the aftercare costs in year 2-5 for both "revised base case" and "likely overestimated case" were the same, which were potentially underestimated due to lack of consideration for costs of device replacement due to reasons other than pump thrombosis (for further details, refer Section: Incidence of device replacement).

The resubmission ADAR argued that all patients were anticipated to be privately insured because the intervention was listed on the Prescribed List, and hence any aftercare hospital costs will be funded by the private insurer. The department considered this to be uncertain as patients will present to public hospitals for disease related complications post LVAD implantation, in which scenario the cost may be borne by the relevant public site. Furthermore, private insurers generally do not cover aftercare costs other than potentially costs associated with technical device monitoring or repeat surgical interventions. Therefore, aftercare costs may be borne by the relevant public site or potentially billed to the patient. This remains unknown. Based on the consultation conducted by the applicant, no feedback was provided by the clinical experts with regard to private health funding in aftercare services and disease related complications (MSAC Application 1749 Resubmission Attachment 2). Furthermore, the resubmission ADAR did not address as to how private patient funding will be attended (for aftercare) by the public hospitals.

The commentary proposed that the aftercare costs were underestimated because of the following reasons:

- Costs associated with device replacement and reoperation as a result of device malfunction apart from pump thrombosis over the proposed 10-year time horizon were not included in the "revised base case".
- Rehabilitation costs were not included. Based on the 2023 International Society for Heart and Lung Transplantation (ISHLT) guidelines[17] for mechanical circulatory support, all patients with durable mechanical circulatory support should be enrolled in cardiac rehabilitation after LVAD implantation. The ISHLT Guidelines[20] for mechanical circulatory support recommended multidisciplinary approach in the cardiac rehabilitation, which include exercise and strength training; smoking cessation strategies; nutritional and dietary modifications; monitoring of LVAD system; and coordination with the transplant centres for recommendations.
- Referring to Section 3 LVAD CEA Workbook of MSAC Application 1749 Resubmission ADAR, the cost for "other neurological event" under the "disease related costs" in the LVAD arm was omitted in the model. Also, the antihypertensive management was updated to $414.07 during the commentary, as it was incorrectly presented in the resubmission ADAR using 356.25 days. Therefore, by incorporating the cost for "other neurological event and updated costs for antihypertensive management, the ICER increased by about 4% to $redacted/QALY.

Consultation with local clinical experts on aftercare costs in Australia

In response to MSAC advice, the applicant conducted consultations with clinicians from all four adult transplant centres and a non-transplant centre regarding the expected magnitude of LVAD aftercare costs. The methods of the consultations included interviews and a survey (the survey allowed for free-text comments and multiple-choice options of "uncertain"), where local experts were consulted on the comparison between the resource utilisation as reported in Prichard et al., 2020 and Marasco et al., 2016, with the consideration of time period (contemporary practice vs 2012-2014), intended use (DT vs BTT/BTC) and generation of device (HM3 vs older generation LVAD). The applicant also presented a US-based study by Mehra et al., 2018[18] to the local experts to inform the relative magnitude of LVAD aftercare costs in DT vs BTT/BTC and HM3 vs older generation devices (HM2/HVAD/VentrAssist). Mehra et al., 2018 found the aftercare costs

[17] Saeed D, Feldman D, El Banayosy A et al. The 2023 International Society for Heart and Lung Transplantation Guidelines for Mechanical Circulatory Support: A 10- Year Update. The Journal of Heart and Lung Transplantation 2023;42(7):e1-222 https://www.jhltonline.org/article/S1053-2498(22)02248-3/fulltext

[18] Mehra MR, Salerno C, Cleveland JC et al. Healthcare Resource Use and Cost Implications in the MOMENTUM 3 Long-Term Outcome Study. Circulation 2018 Oct 30;138(18):1923-1934. doi: 10.1161/CIRCULATIONAHA.118.035722.

in patients implanted with HM3 for DT to be 60% lower than patients implanted with HM2 for BTT/BTC.

Table 7 presents the post-index hospitalisation costs from Prichard et al., 2020; Marasco et al., 2016; and Mehra et al., 2018.

Table 9 Aftercare costs based on Prichard et al., 2020; Marasco et al., 2016; and Mehra et al., 2018.

	Prichard et al., 2020	**Marasco et al., 2016**	**Mehra et al., 2018**			
Setting, years of data collection	Australia, 2009-2012	Australia, July 2010-June 2012	*United States, Sept 2014-Aug 2016*		*United States, Sept 2014-Aug 2016*	
Population (number of patients)	BTT/BTC (n=25)	BTT/BTC (n=24)	BTT/*BTC (n=137)*		DT *(n=200)*	
LVAD device	HVAD (n=25)	HeartMate II (n=5); HVAD (n=8); VentrAssist (n=11)	HeartMate II (n=62)	HeartMate 3 (n=75)	HeartMate II (*n=98*)	HeartMate 3 (n=102)
Total costs per patient per year (median)	AUD$ 39,130[a]	AUD$ 11,669[a]	USD$ 82,751[b] *(AUD$ 149,902[c])*	USD$ 47,053[b] *(AUD$ 85,236[c])*	USD$ 70,751[b] *(AUD$ 128,164[c])*	USD$ 33,423[b] *(AUD$ 60,545[c])*

Source: Table 11, pp29-30; and Table 12, p31 of MSAC Application 1749 Resubmission ADAR.
BTC = bridge to candidacy; BTT = bridge to transplant; DT = destination therapy; HVAD = HeartWare ventricular assist device; LVAD = left ventricular assist device; n = number of participants.
Notes: Italics added during commentary.
[a] Costs were inflated to 2024 AUD prices.
[b] *Costs were presented in 2017 USD prices in the Mehra et al., 2018.*
[c] *Costs were inflated and converted to 2024 AUD prices based on the conversion rate of USD$1 to AUD$1.45 (https://eppi.ioe.ac.uk/costconversion/default.aspx)*

A total of five clinicians participated in the survey. Four of them were heart failure and transplant cardiologists from implant centres in Queensland, Western Australia, Victoria and New South Wales. A cardiologist/heart failure specialist from a non—implanter centre was also involved in the feedback consultations. The key results from the survey were:

- All five clinicians responded that the contemporary LVAD aftercare costs were below $39,130.03 (cost inflated from Prichard et al., 2020), with 3 out of 5 clinicians expressed the costs to be between $11,669.22 (cost inflated from Marasco et al., 2016) and $39,130.03.
- All five clinicians agreed that aftercare costs with DT were lower than in BTT/BTC.
- All five clinicians concurred that aftercare costs with HM3 would be lower, compared to older generation LVAD such as HM2 and HVAD.
- All respondents considered that the magnitude of aftercare costs would be lower in subsequent years compared to the first year after implant.
- All five clinicians agreed that $redacted aftercare costs in the first year after index hospitalisation would be an outlier in the Australian LVAD setting.

Overall, the results of the survey supported the magnitude of LVAD aftercare costs applied in the original submission ADAR which was approximately between Marasco et al., 2016 and Prichard et al. 2020 ($11,669.22 to $39,130.03). However, the commentary considered that the aftercare costs from Prichard et al., 2020 were underestimated as the study reported $0 in rehabilitation costs and $0 in "other hospital" costs (as defined by all costs reported outside the

implant hospital) after LVAD implantation. Based on the data from Moghei M et al., 2019[19], a cross-sectional multinational study including Australia, which characterised the costs of cardiac rehabilitation, the mean cost of a cardiac rehabilitation program following an acute cardiac event or hospitalisation was USD $1,024, which was approximately AUD $1,890 (adjusted to AUD 2024 price). That cost was driven by personnel, exercise equipment and stress testing[19]. The commentary also noted that LVAD patients after implantation may incur additional costs outside the implant centres such as routine LVAD care, driveline evaluation, routine laboratory testing and cardiac rehabilitation[20], especially those who live remotely or away from the implant centres.

Regarding the format of aftercare services (e.g. in-person, telehealth and/or hybrid), three of the clinicians, who were additionally consulted by the applicant via informal individual interviews, were not able to provide a breakdown of the format of aftercare services. The clinicians emphasised that the format is dependent on clinical best practice and patient preference or situation, with in-person aftercare services as the preferred format, and telehealth or hybrid consult for patients living remotely. The informal interviews with clinicians revealed that the costs of aftercare services, regardless of the format, were included in the overall aftercare costings post LVAD implantation. Of note, the costing for private-funded patients who obtain aftercare services at the public hospital was unaddressed. It was uncertain if these patients will be funded by private insurance or public hospital system or out-of-pocket payment.

Overall, the resubmission ADAR's approach in obtaining contemporary and informed estimates of the aftercare costs post LVAD implantation from Australian hospitals was inadequate as it only involved consulting with Australian clinical experts to validate the aftercare costs based on two published studies, Prichard et al., 2020 and Marasco et al., 2016. The commentary considered that a micro-costing approach to obtain the actual costs of post LVAD implantation may be more accurate.

Results of revised base case and likely overestimated case analysis

Based on the resubmission ADAR, the cost of the index admission for HM3 implantation was $redacted per patient, which included the costs associated with the HM3 LVAD implant surgery and implant kit ($redacted) and costs associated with the implant procedure and recovery ($76,480, this cost has been inflated to AUD 2024. The cost presented in the original ADAR for this is $72,163.79).

Table 8 presents the stepped economic analysis for the applicant-proposed "revised base case" and "likely overestimated case" results of the economic evaluation.

[19] Moghei M, Pesah E, Turk-Adawi K et al. Funding sources and costs to deliver cardiac rehabilitation around the globe: Drivers and barriers. Int J Cardiol 2019 Feb 1;276:278-286. doi: 10.1016/j.ijcard.2018.10.089

Table 10 Results of the stepped economic analysis

Step	HM3	OMM	Increment	ICER
Original ADAR base case (Trial-based costs and outcomes with lifetime horizon)				
Costs QALY	$**redacted** 4.929	$87,522 0.258	$**redacted** 4.671	$**redacted** [a]
Revised base case				
Step 1 – Time horizon of 15 years				
Costs QALY	$**redacted** 4.291	$87,522 0.258	$**redacted** 4.034	$**redacted**
Step 2 – Time horizon of 15 years and utility values of 0.64 (OMM and LVAD arm first cycle, and OMM arm subsequent cycles)				
Costs QALY	$**redacted** 4.300	$87,522 0.375	$**redacted** 3.925	$**redacted**
Step 3 – Time horizon of 15 years; utility values of 0.64 (OMM and LVAD arm first cycle, and OMM arm subsequent cycles); and annual risk of device replacement (Years 0-2 = 0.01; Years 2+ = 0.011)				
Costs QALY	$**redacted** 4.300	$87,522 0.375	$**redacted** 3.925	$**redacted**
Step 4 – Time horizon of 15 years; utility values of 0.64 (OMM and LVAD arm first cycle, and OMM arm subsequent cycles); annual risk of device replacement (Years 0-2 = 0.01; Years 2+ = 0.011); and OMM first cycle cost = $4,958.11				
Costs QALY	$**redacted** 4.300	$72,557 0.375	$**redacted** 3.925	$**redacted**
Step 5 – Time horizon of 15 years; utility values of 0.64 (OMM and LVAD arm first cycle, and OMM arm subsequent cycles); annual risk of device replacement (Years 0-2 = 0.01; Years 2+ = 0.011); OMM first cycle cost = $4,958.11; and aftercare costs = $19,489.46 per year in months 0-24.				
Costs QALY	$**redacted** 4.300	$72,557 0.375	$**redacted** 3.925	$**redacted**
Likely overestimated case				
Step 1 – Time horizon of 10 years				
Costs QALY	$**redacted** 3.648	$87,522 0.258	$**redacted** 3.391	$**redacted**
Step 2 – Time horizon of 10 years and utility values of 0.64 (OMM and LVAD arm first cycle, and OMM arm subsequent cycles)				
Costs QALY	$**redacted** 3.648	$87,522 0.375	$**redacted** 3.282	$**redacted**
Step 3 – Time horizon of 10 years; utility values of 0.64 (OMM and LVAD arm first cycle, and OMM arm subsequent cycles); and annual risk of device replacement (Years 0-2 = 0.01; Years 2+ = 0.022)				
Costs QALY	$**redacted** 3.657	$87,522 0.375	$**redacted** 3.282	$**redacted**
Step 4 – Time horizon of 10 years; utility values of 0.64 (OMM and LVAD arm first cycle, and OMM arm subsequent cycles); annual risk of device replacement (Years 0-2 = 0.01; Years 2+ = 0.022); and OMM first cycle cost = $0				
Costs QALY	$**redacted** 3.657	$70,078 0.375	$**redacted** 3.282	$**redacted**
Step 5 – Time horizon of 10 years; utility values of 0.64 (OMM and LVAD arm first cycle, and OMM arm subsequent cycles); annual risk of device replacement (Years 0-2 = 0.01; Years 2+ = 0.022); OMM first cycle cost = $0; and aftercare costs = $39,130.03 per year in months 0-24				
Costs QALY	$**redacted** 3.657	$70,078 0.375	$**redacted** 3.282	$**redacted**

Source: Table 20, pp38-39; Table 23, p40 of MSAC Application 1749 Resubmission ADAR.
HM3 = HeartMate 3: ICER = incremental cost-effectiveness ratio; LVAD = ventricular assist device; OMM = optimal medical management; QALY = quality-adjusted life year.
Notes: [a] ICER was updated in the resubmission ADAR based on price changes in the MBS and PBS items as of August 2024, and costs adjustment for inflation using the 2024 AIHW index. The ICER for the base case presented in the MSAC Application 1749 ADAR was originally $41,796.

The original base case ICER was $**redacted** the ICER for the base case of $**redacted** which was reported in the MSAC Application 1749 was updated based on price changes in the MBS and PBS items as of August 2024, and costs adjustment for inflation using the 2024 AIHW index.

The resubmission ADAR presented an ICER of $**redacted** per QALY for the "revised base case" (time horizon 15 years; utility value of 0.64 in all OMM cycles and LVAD first cycle; annual risk of device replacement of 0.01 EPPY in Years 0-2 and 0.011 EPPY in Years 2+; OMM first cycle cost of $4,958.11; annual aftercare cost of $**redacted** in LVAD arm in the first 2 years).

The resubmission ADAR also presented a stepped economic analysis for the "likely overestimated case". Based on the resubmission ADAR, a device replacement rate of 0.022 EPPY was proposed in year 2-5 in the "likely overestimated case". However, this rate was applied to the "suspected or confirmed pump thrombosis" in the economic model, as presented in Section 3 LVAD CEA Workbook of MSAC Application 1749 Resubmission ADAR. Of note, "suspected or confirmed thrombosis" incurred a cost of $15,474.83, while the "pump thrombosis resulting in reoperation" incurred a cost of $**redacted** in the economic model. By applying the rate of 0.022 EPPY to "suspected or confirmed pump thrombosis" and not to "pump thrombosis resulting in reoperation", the resubmission ADAR underestimated the cost of device related events. By applying the rate of 0.022 EPPY to "pump thrombosis resulting in reoperation", the ICER increased from $**redacted** to $**redacted** per QALY (Step 3). The resubmission ADAR acknowledged that the time horizon and aftercare costs impacted the results of the economic evaluation. The disaggregated costs for LVAD vs OMM in both "revised" and "likely overestimated case" are presented in Table 9.

Table 11 Disaggregated costs (discounted)

Cost item	LVAD	OMM	Incremental
Revised base case			
Pre-implant procedural costs	$22,428	$22,428	$0
LVAD procedural costs	$**redacted**	$0	$**redacted**
Device costs[a]	$**redacted**	$0	$**redacted**
Implant and post implant procedural costs	$76,480	$0	$76,480
Aftercare costs			
Ongoing management[b]	$9,612	$967	$8,645
Rehabilitation	*NA*	*NA*	*NA*
Device related event costs	$**redacted**	$0	$**redacted**
Disease related event costs	$35,094	$49,162	-$14,068
Total	$**redacted**	$72,557	$**redacted**
Likely overestimated case			
Pre-implant procedural costs	$22,428	$22,428	$0
LVAD procedural costs	$**redacted**	$0	$**redacted**
Device costs[a]	$**redacted**	$0	$**redacted**
Implant and post implant procedural costs	$76,480	$0	$76,480
Aftercare costs			
Ongoing management[b]	$8,165	$967	$7,199
Rehabilitation	*NA*	*NA*	*NA*
Device related event costs	$**redacted**	$0	$**redacted**
Disease related event costs	$40,436	$46,683	-$6,247
Total	$**redacted**	$70,078	$**redacted**

Source: Table 21 of p39; and Table 23 of p40 of MSAC Application 1749 Resubmission ADAR.
HM3 = HeartMate 3; LVAD = ventricular assist device; OMM = optimal medical management; NA = not available.
Notes: [a] Includes HM3 LVAD + implant kit. [b] Includes ECG, clinic visit, anticoagulation and antihypertensive management.
Italics added during commentary.

Table 10 summarises the incremental cost-effectiveness for LVAD vs OMM.

Table 12 Incremental cost-effectiveness for LVAD vs OMM

Parameter	LVAD	OMM	Increment
Revised base case			
Costs	$**redacted**	$72,557	$**redacted**
Life years	5.451	0.586	4.865
QALYS	4.300	0.375	3.925
Incremental cost per life year gained			***$redacted***
Incremental cost per QALY gained			$**redacted**
Likely overestimated case			
Costs	$**redacted**	$70,078	$**redacted**
Life years	4.637	0.586	4.051
QALYS	3.657	0.375	3.282
Incremental cost per life year gained			***$redacted***
Incremental cost per QALY gained			$**redacted**

Source: Table 25 of p41; Table 26 of p41 of MSAC Application 1749 Resubmission ADAR.
HM3 = HeartMate 3: OMM = optimal medical management; QALY = quality-adjusted life year.
Notes: Italics added during commentary.

The commentary considered that the incremental cost per QALY in the "revised base case" and "likely overestimated case" were underestimated because the aftercare costs did not include rehabilitation costs (as provided by allied health workers) for patients who received LVAD implantation, as well as potential underestimation in the rate of pump replacement over a 10- or 15-year time horizon, as a result of pump thrombosis, device malfunction and infection.

Uncertainty analysis: Model inputs and assumptions

The key drivers of the model are presented in Table 11.

Table 13 Key drivers of the model

Description	Method/Value	Impact Revised base case: $redacted/QALY gained
Time horizon	Treatment effect continued beyond the 5-year trial period for up to 15 years.	High, favours LVAD Using a time horizon of 5 years increased the ICER to $**redacted** /QALY gained.
LVAD device cost	High value of LVAD device cost, which included private health funded LVAD implant kit and HM3 Mini Apical Cuff Kit, as well as the Patient Support Kit Bundle[a]	High, favours OMM Using a device cost of $**redacted** reduced the ICER to $**redacted** [b]/QALY gained
Procedural and recovery costs	High value for implant procedure and post-recovery costs from Prichard et al., 2020	High, favours OMM Use of a lower procedural and recovery cost of $38,240.02 reduced the ICER to $**redacted** [b]/QALY gained.
Health state utility in LVAD arm for subsequent cycles	High value for model health states taken from Sato et al., 2022 and no disutility for adverse events.	High, favours LVAD Use of lower health state utility 0.59 for LVAD subsequent cycles increased the ICER to $**redacted** [b]/QALY gained.

Source: Table 27, pp43-45 of MSAC Application 1749 Resubmission ADAR.
HM3 = HeartMate 3; ICER = incremental cost-effectiveness ratio; LVAD = left ventricular assist device; OMM = optimal medical management; QALY = quality-adjusted life year.
Notes: [a] Patient Support Kit bundle at a reduced rate to hospitals relative to the combined cost of individual items was supplied by the sponsor.
[b] These ICERs were not traceable from the Section 3 LVAD CEA Workbook of MSAC Application 1749 Resubmission ADAR. However, the differences between the presented ICERs and calculated ICERs by the commentary were minimal, with less than 3% differences.

Univariate sensitivity analyses presented in the resubmission ADAR showed that the model, as per the original model, was most sensitive to the variations in the discount rate, time horizon, LVAD device cost and procedural costs with LVAD implantation. The resubmission ADAR claimed that variations in OMM costs (first and subsequent cycles), LVAD disease and device related costs (month 1-24 and 25+), and ongoing management had minimal impact on the model. The results of key univariate sensitivity analyses are summarised in Table 12.

Table 14 Sensitivity analyses

Analyses	Sensitivity	Incremental cost	Incremental QALY	ICER	% change from revised base case ICER
Revised base case		**$redacted**	**3.925**	**$redacted**	**0%**
Discount rate (revised base case 5%)	0%	**$redacted**	5.235	**$redacted**	–20%
	3.5%	**$redacted**	4.256	**$redacted**	–6%
Time horizon (revised base case 15 years)	5 years	**$redacted**	2.090	**$redacted**	71%
	10 years	**$redacted**	3.282	**$redacted**	16%
	20 years	**$redacted**	4.281	**$redacted**	-7%
LVAD device cost (revised base case **$redacted**)	**$redacted** (50% less than revised base case)	**$redacted** [f]	3.925	**$redacted**[f]	–29%
	$redacted (50% more than revised base case)	**$redacted**[f]	3.925	**$redacted**[f]	27%
Procedural and recovery costs (revised base case $76,480.04)	$38,240.02 (50% less than revised base case)	**$redacted** [f]	3.925	**$redacted**[f]	–17%
	$114,720.06 (50% more than revised base case)	**$redacted** [f]	3.925	**$redacted**[f]	18%
Health state utility LVAD subsequent cycles (revised base case 0.79)	0.59	**$redacted**	2.857[f]	**$redacted**[f]	37%
	0.99	**$redacted**	4.993[f]	**$redacted**[f]	–21%
Sensitivity analysis performed by the commentary					
Univariate analysis					
*Patient Support Kit Bundle[a] (revised base case **$redacted**)*	***$redacted***	***$redacted***	*3.925*	***$redacted***	*-5%*
	$redacted	***$redacted***	*3.925*	***$redacted***	*-10%*
Annual risk of device replacement in Years 2+ (revised base case 0.011)	*0.022*	***$redacted***	*3.925*	***$redacted***	*+4%*
	0.04	***$redacted***	*3.925*	***$redacted***	*+11%*
Multivariate analysis					
Assuming a time horizon of 10 years[b], OMM disease related costs in the 1st cycle of $0[b], utility value of 0.64[c] for the 1st cycle in both the OMM and the LVAD arms and in subsequent cycles of the OMM arm, utility value of 0.79[c] in the subsequent cycles of the LVAD arm, annual risk of device replacement based on INTERMACS 2023 Annual Report (Years 2+ = 0.04), and aftercare costs $39,130.03[d] per year in months 0-24, with updated cost inputs[e].	***$redacted***	*3.282*	***$redacted***	*+49%*	

Source: Table 27, pp43-45 of MSAC Application 1749 Resubmission ADAR.
ICER = incremental cost-effectiveness ratio; INTERMACS = Interagency Registry for Mechanically Assisted Circulatory Support; LVAD = left ventricular assist device; OMM = optimal medical management; QALY = quality adjusted life year.
Notes:
[a] The sponsor supplies the Patient Support Kit bundle at a reduced rate to hospitals relative to the combined cost of individual items.
[b] Assumptions based on MSAC advice at the April 2024 Meeting.
[c] Utility values were unchanged from applicant-proposed "revised base case" and were consistent with MSAC advice.
[d] Aftercare costs from Prichard et al., 2020, as proposed by the applicant in the "likely overestimated case".
[e] Included cost of "other neurological event" under the "disease related cost" in the LVAD arm and updated cost of antihypertensive management.
[f] These numbers were not traceable from the Section 3 LVAD CEA Workbook of MSAC Application 1749 Resubmission ADAR. However, the differences between the presented ICERs and calculated ICERs by the commentary were minimal, with less than 3% differences.
Italics added during commentary.

Additional univariate sensitivity analyses conducted by the commentary showed that a 50% reduction in the cost of a Patient Support Kit Bundle from $redacted to $redacted, would reduce the ICER by 5% from $redacted/QALY (revised base case) to $redacted/QALY. Based on the resubmission, the Patient Support Kit Bundle was supplied by the sponsor at a reduced rate to hospitals relative to the combined cost of individual items (Section 3 LVAD CEA Workbook of MSAC Application 1749 Resubmission ADAR). In addition, univariate sensitivity analysis performed during commentary suggested that the ICER was sensitive to an increase in annual risk of device replacement from 0.011 to 0.04 EPPY in years 2+ and the ICER increased by 11%, from $redacted to $redacted per QALY.

A multivariate sensitivity analysis was performed by the commentary and the assumptions applied were time horizon of 10 years, OMM disease related costs in the 1st cycle of $0, utility value of 0.64 for the 1st cycle in both the OMM and the LVAD arms and in subsequent cycles of the OMM arm, utility value of 0.79 in the subsequent cycles of the LVAD arm, and annual risk of device replacement (Year 2+ = 0.04 EPPY) based on the INTERMACS 2023 Annual Report. The INTERMACS 2023 Annual Report reported the incidence of device malfunction/pump thrombus 90 days after implantation with HM3 of 0.04 EPPY. With the assumption that all device malfunction/pump thrombosis led to device replacement, the ICER increased by 49% to $redacted/QALY. However, the calculated ICER is uncertain as the assumption on the rate of device replacement was conservative, and a comprehensive aftercare cost was not available based on the applicant-conducted consultation with the Australian hospitals.

Of note, the multivariate sensitivity analysis included the following cost inputs:

- Costs of “other neurological event” – These costs were listed in the Section 3 LVAD CEA Workbook of MSAC Application 1749 Resubmission ADAR but they were not included in total disease related cost in the LVAD arm. Omission of these costs underestimated the disease related costs in the LVAD arm.
- Costs of antihypertensive medications – The total cost of antihypertensive medications was underestimated as the sum presented in the Section 3 LVAD CEA Workbook of MSAC Application 1749 Resubmission ADAR was based on 356.25 days.

14. Financial/budgetary impacts

The resubmission ADAR presented revisions to the financial analysis in response to MSAC advice at the April 2024 Meeting.

In the original submission ADAR, the combined costs of disease and device related complications were excluded from the financial analysis. In the resubmission ADAR, these costs were considered. A sensitivity analysis was conducted in the resubmission ADAR which assigns device and disease related costs to either private insurers or public hospitals. Disease and device related complications are assumed to be incurred by either public or private hospitals (and hence private insurers) as these were classified as Common Terminology Criteria for Adverse Events (CTACAE) grade 3 (or greater) events in the MOMENTUM 3 trial which result in inpatient hospitalisation. It was unclear what proportion of complications would be assigned to either payer, hence a sensitivity analysis was conducted with the assumption of 100% of these costs are incurred by private insurers or public hospitals in order to demonstrate the maximum cost that maybe incurred by either payer.

Table 13 outlines the cost assumptions applied in the financial impact of listing LVAD as DT to various healthcare payers.

Table 15 Data sources and parameter values applied in the financial estimates

Relevant payer	Cost components	Value in original submission ADAR	Value in resubmission ADAR	*Commentary*
MBS	LVAD procedure[a]	$2,846.06 (cost per procedure)	$2,846.06 (cost per procedure)	*This resubmission ADAR did not update the LVAD procedure cost using the current MBS fee[b]. Using the current MBS fee, the cost to MBS was calculated to be $2,959.36, which was a slight increase from the value in original submission ADAR.*
	Incremental costs of ongoing management in LVAD patients versus OMM patients[c]	$3,290.91	$3,909.25	*Increased.* *This is appropriate as the costs were updated as per current MBS fee (update 1st July 2024)*
	Total	$6,136.96	$6,755.31	*Increased.*
PBS	Incremental costs of ongoing management in LVAD patients versus OMM patients[d]	$2,085.52	$2,141.72	*Increased.* *This is appropriate as the costs were updated as PBS DPMQ.*
Private health funds	Device and Total LVAD system cost[e]	$**redacted**	$**redacted**	*No changes.*
	Implant procedure and post-recovery costs[f] (less cost of device[e])	$72,163.79	$73,633.98[g]	*Increased.*
	Battery replacement[h]	$4,592.00	$4,592.00	*No changes.*
	Total	$**redacted**	$**redacted**	*Increased.*
Public hospitals/private insurers	Device and disease related complication costs resulting in hospitalisation	NR	$**redacted**	*Updated.* *This is uncertain as the rate of pump replacement due to other reasons such as infection and device malfunction were not considered.*

Source: Table 29, p48 and Section 4 LVAD budget impact model of MSAC Application 1749 Resubmission ADAR; Table 16, p39 of MSAC 1749 PSD.

DPMQ = dispensed price for maximum quantity; LVAD = ventricular assist device; OMM = optimal medical management; MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Schedule; NR = not reported.

Notes:

[a] The LVAD procedure cost included MBS item 38615 (insertion of a left or right ventricular assist device); 20560 (initiation of the management of anaesthesia); 23230 (anaesthesia/perfusion time units) and 22060 (whole body perfusion, cardiac bypass).

[b] Based on the current MBS item fee (update on 1st July 2024): item 38615 ($1,745.25); 20560 ($451); 23230 ($608.85) and 22060 ($676.50) at the assumption of 85% benefit.

[c] This included MBS items for ongoing monitoring (item 11713 – ECG, item 105 - clinic visit) and international normalised ratio (INR) testing (items 65120, 74995, 3)

[d] This included costs associated with anticoagulation management (warfarin, aspirin) and antihypertensive management (angiotensin-converting enzyme inhibitors [ACEIs], beta-blockers)

[e] This cost includes LVAD implant kit cost, Patient Support Kit Bundle, HM3 Mini.Apical Cuff Kit

[f] Costs based on Prichard et al 2020 and number of days in hospital based on Silbert et al 2023

[g] This amount is the total cost of implant procedure and post-recovery costs ($76,480.04, as in Table 9), excluding the cost of LVAD procedure to MBS ($2,846.06).

[h] $2,296.00 applied to alive LVAD patients every three years

Italics added during commentary

In the original submission ADAR, the total costs to MBS and PBS per LVAD procedure per year were $6,136.96 and $2,085.52, respectively. The sum increased to $6,755.31 and $2,141.72, respectively, in the resubmission ADAR. The commentary calculated the total cost to MBS, based on updated MBS item fees and the total cost was $6,868.61.

Table 14 summarises the incremental costs of device and disease related costs in LVAD patients versus OMM patients. The resubmission ADAR presented the incremental cost of total disease and device related costs resulting in hospitalisation of $redacted over 6 years. The commentary considered that the device related complication costs were underestimated as it did not account for risk of reoperation and pump replacement as a result of device malfunction or infection. It was noted that the price relied on, for the economic and financial analyses, includes the price for any accessories associated with use of the principal device (i.e. $redacted, which was appropriate.

Table 16 Incremental costs of device and disease related costs in LVAD patients versus OMM patients by payer

Parameter	Treatment arm	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Total	Calculation /Source
Device related costs resulting in hospitalisations	LVAD	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted	Calculated based on revised base case analysis – undiscounted, non-half cycle corrected
Disease related costs resulting in hospitalisations	LVAD	$12,857	$11,013	$2,849	$1,917	$1,743	$1,569	$31,948	Calculated based on base case analysis – undiscounted, non-half cycle corrected
	OMM	$31,408	$6,767	$91	$0	$0	$0	$38,266	
Total disease and device related costs resulting in hospitalisations	Incremental	$redacte	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted	LVAD arm – OMM arm

Source: Table 28 of MSAC Application 1749 Resubmission ADAR.
EE = economic evaluation; LVAD = left ventricular assist device; MBS = Medicare Benefits Schedule; OMM = optimal medical management; PBS = Pharmaceutical Benefits Scheme.

Table 15 presents the net financial implications of LVAD as DT to the government health budget, and the numbers were updated by the commentary based on the MSAC Application 1749 Resubmission ADAR Attachment Section 4.

Table 17 Net financial implications of HM3, from the perspective of the government

Parameter	Year 1 2025	Year 2 2026	Year 3 2027	Year 4 2028	Year 5 2029	Year 6 2030
Estimated use and net cost of the proposed health technology (HM3)						
Number of LVAD procedures reimbursed on the MBS for DT	redacted	redacted	redacted	redacted	redacted	redacted
Total cost to the MBS	$redacted [a]	$redacted [a]	$redacted [a]	$redacted [a]	$redacted [a]	$redacted [a]
Total cost to the PBS	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted
Total cost to private health funds	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted
Device and disease related costs resulting in hospitalisation	$redacted	$redacted	$redacted	$redacted	$redacted	$redacted

Source: Developed during the commentary from Section 4 LVAD Budget impact model of the MSAC Application 1749 Resubmission ADAR
DT = destination therapy; HM3 = HeartMate 3; LVAD = left ventricular assist device; MBS = Medicare Benefits Schedule; PBS = Pharmaceutical Benefits Scheme.
Notes: [a]This cost has been updated by the commentary with the total cost to the MBS based on the MBS cost per procedure of $6,868.61, as identified above.

The net costs to MBS over 6 years was $redacted (original submission ADAR), and it increased by 12% to $redacted (resubmission ADAR). As for the net costs to PBS, the net cost in the original submission ADAR was $redacted, and it increased by 2.7% to $redacted in the resubmission ADAR, over year 1-6. The net costs to private health funds increased minimally in the resubmission ADAR. The financial impact to private health funds was estimated to be $redacted in year 1 increasing to $redacted in year 6. The device and disease related costs resulting in hospitalisation increased from $redacted in year 1 to $redacted in year 6, with the assumption that the payer was solely either the public hospitals or private health insurers. Of note, the net financial implications were uncertain because the analysis did not include the aftercare costs of rehabilitation (as provided by nursing and allied health staff) and device related costs (risk of device replacement due to reasons other than pump thrombosis).

15. Other relevant information

The resubmission ADAR did not present other relevant information.

16. Applicant comments on MSAC's Public Summary Document

Abbott Australasia Pty Ltd. (Abbott) welcomes the MSAC's decision to provide public funding for LVADs for DT patients. Abbott is dedicated to collaborating with all relevant stakeholders to facilitate the earliest possible implementation of the MBS item, ensuring timely access for patients in need.

17. Further information on MSAC

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