Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1398 – Implantation of a permanent leadless and batteryless haemodynamic sensor and associated remote analysis of pulmonary artery pressure for patients with moderate chronic heart failure (New York Heart Association class III)

Applicant: **Optum on behalf of St. Judes Medical Australia**

Date of MSAC consideration: **MSAC 65th Meeting, 26 November 2015**

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, see at www.msac.gov.au

1. Purpose of application and links to other applications

A submission-based assessment report (the application) requesting Medicare Benefits Schedule (MBS) listing of a wireless pulmonary artery pressure sensor for patients with moderate chronic heart failure was received from St. Jude Medical Australia Pty Ltd by the Department of Health in June 2015.

2. MSAC's advice to the Minister

After considering the available evidence in relation to safety, clinical effectiveness and cost-effectiveness, MSAC deferred its advice for public funding for a permanent leadless and batteryless haemodynamic sensor and associated remote analysis of pulmonary artery pressure for patients with moderate chronic heart failure (NYHA class III) for at least 3 months regardless of ejection fraction, a stable and optimised medication regimen, and a heart failure-related hospitalisation within the previous 12 months.

MSAC recommended reconsideration of the application via the Evaluation Sub-Committee (ESC) after the Prostheses List Advisory Committee (PLAC) has reviewed the recommendation of the Cardiac Prostheses Clinical Advisory Group (CPCAG) to not support inclusion of the device in the Prostheses List, and when economic analyses have been re-evaluated and the patient selection has been clearly delineated.

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

MSAC considered the application for a leadless and batteryless pulmonary artery pressure sensor for patients with moderate chronic heart failure (NYHA III). MSAC agreed that a

clinical need for the device was established with this patient population still experiencing moderate symptoms and remaining at 10-15% risk of death within a year despite optimal care.

Issues with the descriptor were identified that require clarification:

- whether to describe the device more precisely as a pulmonary artery pressure sensor rather than a haemodynamic sensor;
- possible separation of MBS items to insert, remove and replace the device (noting that the last of these items would not be consistent with the applicant's assumption of one device inserted per lifetime);
- whether to more closely align the MBS eligible patient population to that defined for recruitment into the key trial (CHAMPION);
- qualifications and competencies of the clinicians performing the implantation via a catheter and interpreting the device output in order to modify subsequent treatment.

Issues with the identification of how best to optimise the delivery of the proposed service were identified that also require clarification:

- definition of which centres should provide this service and by what criteria they should be identified;
- definition of who should perform the remote monitoring of the haemodynamic sensor output and by what criteria these individuals should be identified;
- definition of any entities which should not receive the haemodynamic sensor output for privacy reasons (such as the device manufacturer);
- clearer statement of the optimal frequency of specialist consultations following the insertion of the haemodynamic sensor, and of the rationale for this frequency (noting that the pre-MSAC response reported that the CHAMPION trial protocol provided for consultations at 1, 3 and 6 months and then 6-monthly, and clinicians logged in to access pulmonary arterial pressure data 2.5 times per patient per week, which reduced to once weekly when the patient stabilised).

The current clinical management algorithm for this patient group is complex thus leading to variability in standard care practices which may contribute to variations in the likelihood of being hospitalised. MSAC agreed on the importance of defining current standard care for this patient population for use as the comparator for care that would also involve the proposed device.

The applicant's literature review identified a single randomised controlled trial (CHAMPION) upon which safety and clinical effectiveness of the device were assessed. An additional three randomised trials might be relevant (COMPASS-HF, REDUCE-HF and LAPTOP-HF), but were not central to the MSAC deliberations because they assessed haemodynamic function in other parts of the heart, and also because they involved haemodynamic sensors containing batteries and leads. MSAC noted that these other trials produced less favourable results, and considered that a meta-analysis of all four trials would likely result in less favourable estimates of improved patient outcomes for haemodynamic sensors more broadly compared with the pulmonary artery pressure sensor alone.

MSAC noted that the pulmonary artery pressure sensor was at least non-inferior to standard care, however longer-term safety and rate of device failure was unclear beyond the nonrandomised extension of the CHAMPION trial to a total mean duration of follow-up of 31 months. In addition, MSAC agreed that the pulmonary artery pressure sensor was effective at decreasing heart failure-related hospitalisations, but the trial was underpowered to confirm

any effect on mortality to conventional standards of statistical significance, as suggested by the favourable trend. A statistically significant reduction in all-cause admissions to hospital was reported after an 18-month mean duration of follow-up in the article by Abraham et al in the Lancet, 8 November 2015 (hazard ratio of 0.84, 95% confidence interval of 0.75 to 0.95).

MSAC noted that measures to minimise bias in the CHAMPION trial seemed reasonable, but noted the following limitations in its design which highlighted areas of clinical uncertainty that MSAC were concerned with:

- the non-comparative nature of any safety assessment due to implanting the device in both the control and treatment groups (the reduced safety of adding at least one more procedure to the patient's management was not sufficient to doubt the overall safety profile);
- the limitations associated with single-blind assessment of subjectively determined outcomes (although 74% of trial participants were hospitalised via an emergency department admission, which gave some degree of confidence to these results);
- the short-term time frame of 15.2 months mean duration of extended follow-up (noting that this was extended to 18 months mean duration of follow-up of the randomised trial in the article by Abraham et al in the Lancet, 8 November 2015);
- the external validity to the proposed MBS eligible patient population, including from a trial conducted in a health care system with different definitions of standard care, and with different thresholds for hospitalisation, but noting from the pre-MSAC response that there was no signal for reduced effectiveness in the subgroup of CHAMPION participants who were aged 65 years or older;
- any effect on mortality was not established.

MSAC noted that the estimate of quality-adjusted life-years (QALYs) gained was driven by the numerically improved survival and symptom benefit over the modelled lifetime time horizon (and 5 years) extrapolated from the CHAMPION study. Furthermore, the main contributor to the cost per patient was the hospitalisation for the procedure and the hospital's monitoring system equipment. MSAC noted that the cost for ongoing monitoring of the pulmonary artery pressure by the clinician was absorbed by standard care and therefore was not accounted for in the economic modelling.

The economic evaluation resulted in a moderate incremental cost-effectiveness ratio of $25,163/QALY for the base case of the model. MSAC noted that the key drivers of the model indicated by the sensitivity analyses were the baseline rate of heart failure-related hospitalisations; the extent of effects on heart failure-related hospitalisation, mortality and utility; the cost of the device implantation; and the costs associated with heart failure-related hospitalisation.

It was unclear whether the pulmonary artery pressure sensor is cost-effective with several areas of uncertainty identified including:

- costs associated with training and monitoring;
- additional workup costs;
- assumptions of survival benefit;
- assumptions of ongoing quality of life benefit beyond 12 months;
- the method of applying utilities in the Markov model, which had the implausible effect of improving quality of life in patients in the intervention arm.

MSAC agreed that, although it was reasonable to assume a single insertion over a patient's lifetime, incremental costs associated with aspirin therapy and complications associated with

aspirin therapy, and incremental costs associated with training and monitoring should also be included in the economic analysis.

MSAC considered that the estimate of likely patient numbers (48–960) may be conservative. The financial impact to the government, calculated to be $1.3 million in year one increasing to $27.6 million in year five, was therefore a likely underestimation. Uptake of the device was also likely to be underestimated unless the eligible population is more clearly restricted by clinical criteria or by limiting the access only to accredited sites of excellence. MSAC therefore considered whether it would be a better investment to improve outcomes with standard care by improving current disease management strategies and access to care teams.

In deferring the application, MSAC requested that the following issues be addressed in particular:

- definition of which centres should provide this service and by what criteria they should be identified;
- definition of who should perform the remote monitoring of the haemodynamic sensor output and by what criteria these individuals should be identified;
- definition of any entities which should not receive the haemodynamic sensor output for privacy reasons (such as the device manufacturer);
- clearer definition of the 'standard of care' for chronic heart failure as the comparator for the haemodynamic sensor;
- clearer statement of the extent to which the frequency of specialist consultations would vary with the introduction of the haemodynamic sensor, and of the rationale for this expected change in frequency;
- reconsideration of economic model uncertainties – particularly in relation to the method of applying utilities, and the need to include the costs of training and monitoring.

4. Background

This technology has not been considered previously by MSAC.

5. Prerequisites to implementation of any funding advice

The application identified the CardioMEMS PA Sensor and Delivery System model CM2000 (AIMD class, ARTG number 236015) and the CardioMEMS Hospital Electronics System CM3000 (Class III, ARTG number 236016), which were listed on the ARTG in April 2015, and that it was anticipated that the i3 patient electronics system (Class I medical device) would receive TGA approval in Q3 2015.

Consultation feedback from a competing device manufacturer at the PASC stage advocated for a generic process and listing, and advocated for changes to the technology description. PASC decided to accept the revised Protocol's description of the technology as a permanent leadless and batteryless haemodynamic sensor.

The independent critique noted that CardioMEMS was one type of pulmonary artery sensor and that the proposed medical service item would apply to all future sensor devices that become available in Australia. However, the current assessment was limited to consideration of haemodynamic sensors which are both leadless and batteryless.

6. Proposal for public funding

The application requested listing of the insertion, removal, and replacement of a permanent leadless and batteryless haemodynamic sensor in one proposed MBS item. Table 1 sets out the proposed MBS item descriptor and restrictions on the use of the proposed intervention.

The application noted that there are two components to the overall medical service, one to implant the sensor and another to monitor the data from the device. However, the application only requested MBS listing for the insertion, removal and replacement of a permanent leadless and batteryless sensor based on the assumption that remote monitoring of pulmonary artery pressure data would be incorporated into standard care heart failure (HF) management programs. This assumption was supported by the Protocol Advisory Sub-Committee (PASC).

Table 1: Proposed MBS item descriptor

Category 3 – Therapeutic Procedures
MBS Item number XXXX PERMANENT LEADLESS AND BATTERYLESS PULMONARY ARTERY PRESSURE SENSOR, insertion, removal and replacement of, for patients with a diagnosis of moderate HF (NYHA class III) for at least 3 months regardless of ejection fraction, a stable and optimised medication regimen, and a HF-related hospitalisation within the previous 12 months. Criteria for a HF-related hospitalisation includes: (a) a hospitalisation during which a patient is admitted for HF or HF is the primary reason for admission; and (b) the patient displays signs and symptoms of HF on admission; and (c) the use of intravenous diuretic, vasodilator, inotropic, or ultrafiltration therapy is required for the purposes of treating HF. The augmentation of oral therapy may be allowable for defining the admission as HF, if no other reasonable diagnosis can be attributed to the admission.
Fee: $816.60 Benefit: 75% = $612.45 Benefit: $85% = $694.10

Source: Table A.2-1, p18 of the application
HF = heart failure; NYHA = New York Heart Association

ESC noted that the descriptor did not specify who should perform the implantation or the qualifications required, but the final protocol had indicated initial uptake of the system would likely be led by cardiologists who are also heart failure specialists. ESC also noted from the final Protocol that general cardiologists, cardiac surgeons, and electro-physiologists could manage aspects of the system, whilst the monitoring service component could be led by specially trained nurses. However, ESC noted that no monitoring item had been proposed in the application.

The proposed MBS item was specific to those patients with a diagnosis of moderate heart failure (NYHA class III) for at least three months (regardless of ejection fraction), a stable and optimised medication regimen, and a heart failure-related hospitalisation within the previous 12 months.

7. Summary of Public Consultation Feedback/Consumer Issues

No consumer impact statement was provided and no consumers or consumer groups provided feedback during the consultation stage of the Protocol Advisory Sub Committee (PASC) process.

8. Proposed intervention's place in clinical management

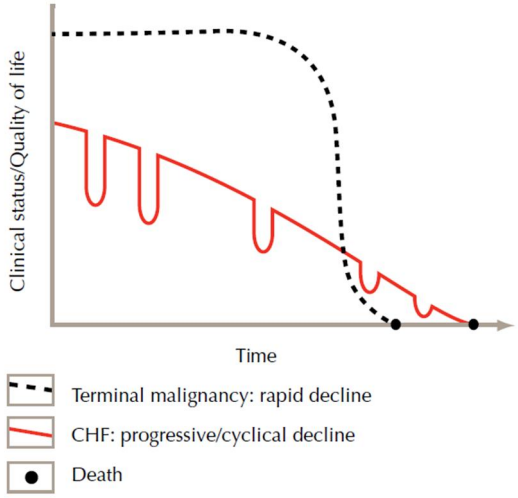
The service proposed for MBS listing was the implantation, removal and replacement of a haemodynamic sensor system for patients with moderate heart failure. The proposed system contains a permanent leadless and batteryless sensor and external home electronics unit that

receives the pulmonary artery pressure transmission from the sensor, and sends the data to a centralised data storage facility. The intervention is intended to provide extra information (i.e. pulmonary artery pressure data) to doctors to better monitor and manage patients with moderate heart failure.

The application stated that:

> Heart failure (HF) (or 'chronic HF' or 'congestive HF) is characterised by insufficient cardiac output to meet the requirements of the body, leading to acute episodes of fluid accumulation often resulting in hospitalisation. HF is a progressive and complex clinical syndrome that is characterised by an underlying structural abnormality or cardiac dysfunction that impairs the ability of the heart ventricle to fill and / or eject blood. HF is mostly a chronic and long-term condition associated with acute episodes of decompensation, and may also develop suddenly. HF can be caused by a number of clinical conditions including ischaemic heart disease, prior myocardial infarction, hypertension and less commonly, non-ischaemic idiopathic dilated cardiomyopathy. Figure 1 shows the typical 'trajectory of illness' associated with HF showing the cyclical and progressive clinical instability following each hospitalisation, which is associated with declining QoL.

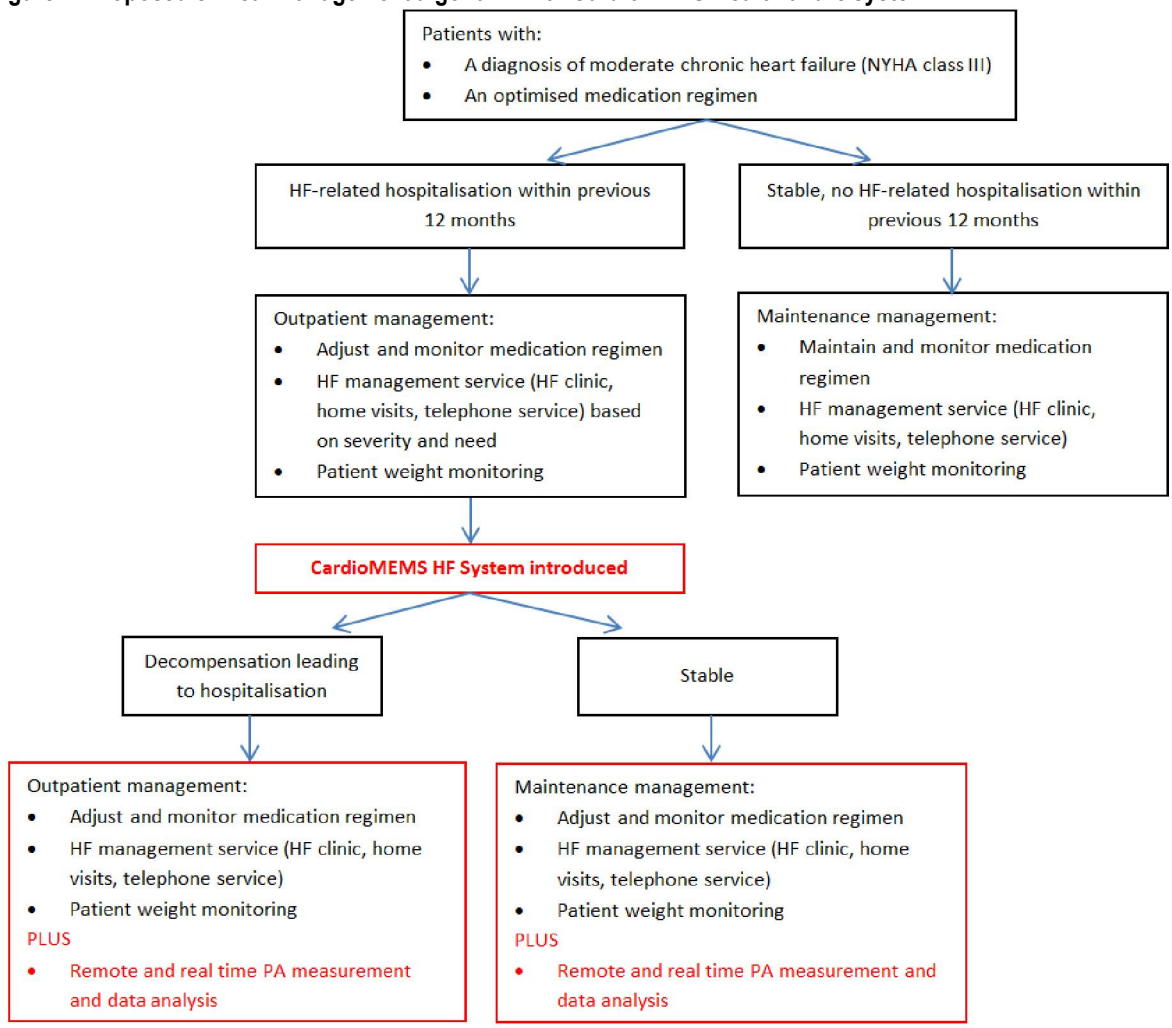
Figure 1: Typical 'trajectory of illness' associated with heart failure



> Early detection of fluid accumulation via real time access to pulmonary artery (PA) pressure changes permits appropriate corrective management to remove fluid, lower intra-cardiac pressures, and thus minimise decompensation requiring hospitalisation. The addition of haemodynamic monitoring to usual outpatient management leads to improved patient outcomes and allows prevention of unnecessary healthcare resource use.

The proposed service would be provided in addition to 'standard care' in line with the clinical management algorithm below.

Figure 2: Proposed clinical management algorithm with CardioMEMS Heart Failure system



Source: Figure A.4-2, p21 of the application
HF = heart failure; NYHA = New York Heart Association; PA = pulmonary artery

9. Comparator

Consistent with the PASC-ratified Protocol, the application nominated 'standard care' as the appropriate main comparator, which includes best practice pharmacotherapy, non-pharmacological strategies, other implantable cardiac devices and heart failure management programs.

10. Comparative safety

The application presented evidence on safety from a single study; the CHAMPION trial. This trial was a prospective, multi-centre, single-blind randomised controlled trial. Participants in both groups were implanted with the sensor. The intervention and control groups compared patients with and without the assessment of haemodynamic sensor readings.

The application presented two main safety endpoints (device-related or system-related complications and pressure sensor failure) as well as an analysis of adverse events, including device; procedure-related; anticipated; serious; and non-serious adverse events. The application noted that all adverse events were treated by established standards of care that protected the life and safety of the participants.

The independent critique considered that, as the main function of the haemodynamic sensor is measuring pulmonary artery pressure for monitoring early signs of heart failure, the primary efficacy and safety outcomes were necessary but insufficient. The critique considered that all-cause hospitalisation and overall survival were important outcomes for this technology.

A summary of serious events for the CHAMPION trial is presented in Table 2 below.

Table 2: Overall summary of adverse events up to six month follow-up visit

	Intervention (N=270)		Control (N=280)	
-	Participants (%)	Events (n)	Participants (%)	Events (n)
Unanticipated SADEs	0 (0.0%)	0	1 (0.4%)	1
SADEs	2 (0.7%)	2	0 (0.0%)	0
Non-Serious ADEs	5 (1.9%)	6	7 (2.5%)	11
Anticipated AEs (up to 30 days)	38 (14.1%)	47	31 (11.1%)	34
Anticipated SAEs	0 (0.0%)	0	0 (0.0%)	0
SAEs	121 (44.8%)	339	155 (55.4%)	385
Non-Serious AEs	175 (64.8%)	603	174 (62.1%)	505

Source: Table B.6-6, p46 of the application
ADEs = adverse device events; AEs = adverse events; SADEs = serious adverse device events; SAEs = serious adverse events

The application claimed that the intervention was non-inferior in terms of safety compared to standard care. The independent critique considered that this may not be reasonable because the control arm in the CHAMPION trial was not strictly 'standard care', patients in the control arm were implanted with the device before randomisation, and there were device-related and system-related complications in both arms.

11. Comparative effectiveness

The application presented evidence on the efficacy of the intervention through the CHAMPION trial. The primary efficacy endpoint of the trial was the rate of heart failure-related hospitalisations within six months of implantation. Secondary endpoints included: change in pulmonary artery pressure from baseline, proportion of patients admitted to hospital for heart failure, days alive outside hospital for heart failure and disease-specific quality of life.

The independent critique considered that, although the measures taken by investigators to minimise bias in the comparative randomised trials were sufficient, the risk of bias in the CHAMPION trial was high as the investigators and outcome assessors were not blinded. It also considered that six-month follow-up data may not be sufficient to inform a model with a long duration, but considered the data from the open access period informative for the economic model.

The application excluded two other direct randomised trials: the REDUCEhf trial; and the COMPASS-HF study trial. The independent critique supported exclusion of the REDUCEhf trial, but considered that exclusion of the COMPASS-HF study was inappropriate, and noted that 86% of patients had NYHA class III and the trial was initially powered to satisfy all efficacy and safety endpoints (Bourge et al, 2008). The critique considered that the study's use of negative binomial regression was correct for count data analyses and noted that all other patient characteristics were similar to the CHAMPION trial. ESC supported the applicant's exclusion of this trial on the basis that COMPASS-HF included a patient population with more advanced disease.

ESC noted that the average age of patients in the CHAMPION trial was 61, whereas the target population would be 80 in the Australian setting. This created some uncertainty about

the effectiveness in the Australian population. ESC also noted that the COMPASS-HF trial used a device which was not leadless or batteryless, and would therefore be out of scope according to the Protocol.

Whilst the critique of the assessment raised concerns regarding risk of bias, difference between the control and intervention arms, and statistically significant survival benefits, ESC agreed that the applicant's Pre-ESC responses addressed these concerns.

ESC noted that while the study showed heart failure related hospitalisations were reduced with the haemodynamic sensor, all-cause hospitalisations at six months were not significantly different between the intervention and control arms (due to other cardiac problems and comorbidities).

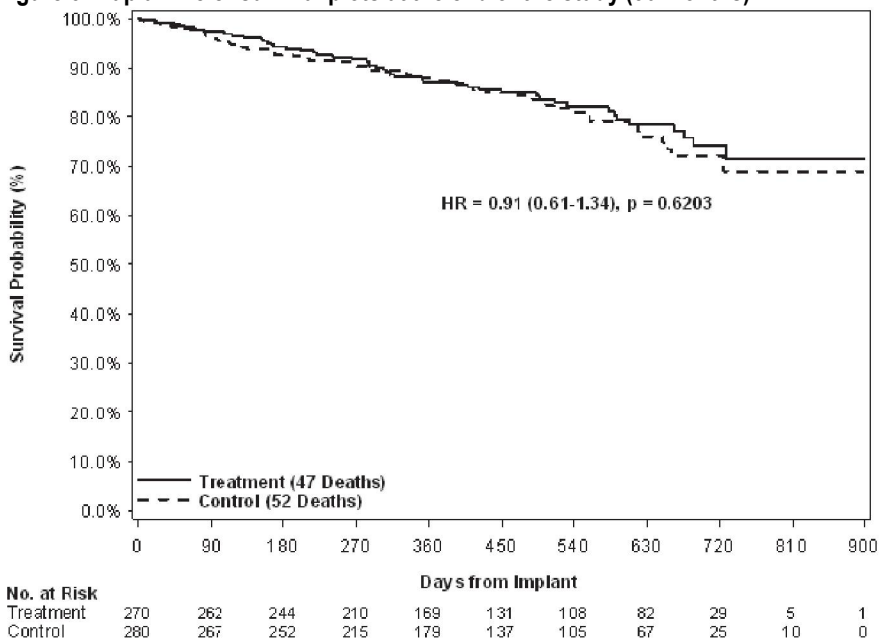
The key efficacy results are presented in Table 3 and Figure 3.

Table 3: Results of efficacy outcomes of the randomised trial CHAMPION

Outcome	Intervention (N=270)	Control (N=280)	Relative risk (95% CI)	p-value
Number of HF-related hospitalisations within 6 months (event/patient)	84 (0.32)	120 (0.44)	0.73 (0.58-0.91)	0.0002
Number of HF-related hospitalisations during randomised follow-up (event/patient) mean follow-up 15.2 months [a]	158 (0.59)	254 (0.91)	0.65 (0.58-0.72)	<0.0001
Number of all-cause hospitalisations within 6 months (event/patient)	232 (0.88)	263 (0.96)	0.91 (not provided)	0.407
Secondary outcomes (at six months)				
Change from baseline in PA mean pressure (mmHg, mean AUC) Median (min, max)	-155.7 -7.2 (-3121, 4783)	33.1 33.7 (-3694, 5726)	NA	0.008
Number of patients admitted to hospital for HF (%)	55 (20.4%)	80 (29.0%)	0.71 (0.53-0.96)	0.029
Days alive outside hospital (days, mean, SD) Median (min, max)	174 ± 31 179 (4, 281)	172 ± 38 178 (48, 201)	NA	0.028
Days hospitalised (days, mean, SD) Median (min, max)	2.2 ± 6.8 0 (0, 66)	3.8 ± 11.1 0 (0, 88)	NA	0.025
Quality of life measured by the Minnesota Living with Heart Failure Questionnaire (mean, SD) [b]	45 ± 26	51 ± 25	NA	0.020

Source: Table B.6-1, p43, Table B.6-4, p45, and Table B.6-3, p44 of the application, Table 8.3 page 125 of trial report.
AUC = area under curve; CI = confidence interval; HF = heart failure; NA = not applicable; PA = pulmonary artery; SD =standard deviation
[a] This is a supplementary endpoint
[b] A lower score indicates improved quality of life

Figure 3: Kaplan-Meier survival plots at the end of the study (30 months)



Source: Figure 8.6, p139 of the Clinical Report
HR = hazard ratio

Based on the evidence from the CHAMPION trial, the application concluded that the haemodynamic sensor was clinically more effective than standard care and non-inferior in terms of safety, compared to standard care.

12. Economic evaluation

The application presented a stepped economic evaluation in the form of a cost-utility analysis using TreeAge Pro 2015. The structure was a lifetime Markov cohort model, with monthly cycles and four health states: (i) standard care and sensor implant, (ii) stable heart failure, (iii) heart failure-related hospitalisation, and (iv) death.

The independent critique considered that the model duration (lifetime) might not be appropriate, noting that extrapolation of outcomes from 17 months to lifetime was problematic and that a shorter model duration would be warranted as patients with moderate heart failure typically have a shorter life expectancy. The critique also noted that the model did not produce similar outcomes to the trial evidence.

The application provided a summary of input parameters included in the economic evaluation (Table 4).

Table 4: inputs to the clinical evaluation

Clinical input parameters	Parameter estimate	
	LAB-IHMS	SOC
Probability of device or procedure related complication	2.6%	NA
Annual HF hospitalisation rate	0.49 (based on RR below)	0.72
Annual RR of hospitalisation for heart failure	0.68	1.00
Annual death rate	0.13	0.16
RR of death	0.79(based on RR below)	1.00
Mean utility at baseline	0.711	0.711
Mean utility of patients from baseline to Month 6	0.719	0.681
Mean utility of patients from baseline to Month 12	0.739	0.660
Cost estimates		
LAB-IHMS procedure	$26,274.92	NA
LAB-IHMS complication	$12,968.00	NA
Hospitalisation for heart failure	$7,672	$7,672
Annual cost of ongoing monitoring	$141	$141
Annual cost OMT	$443	$443

Source: Table E6, pVII of the application
Abbreviations: DSRC device system-related complication; HF, heart failure; OMT, optimised medical therapy; SOC, standard care

Table 5: Results of the economic evaluation

Description	Haemodynamic sensor	Standard care	Difference
Step 1a: 18 months, hospitalisation no discount	-	-	-
Cost	$34,798	$7,098	$27,697
Effect (% hospitalisations)	0.674	0.995	-0.321
Incremental cost per hospitalisation avoided	-	-	**$86,284**
Step 1b: 18 months, QALY, no discounting	-	-	-
Cost	$34,798	$7,098	$27,697
Effect (QALYs)	0.95	0.86	0.09
Incremental cost per QALY	-	-	**$299,743**
Step 2: 5 years, QALY, discounting	-	-	-
Cost	$43,354	$17,933	$25,421
Effect (QALYs)	2.45	2.06	0.39
Incremental cost per QALY	-	-	**$65,895**
Step 3: life time, QALY, discounting	-	-	-
Cost	$53,041	$27,536	$25,505
Effect (QALYs)	4.14	3.13	1.01
Incremental cost per QALY	-	-	**$25,163**

Source: Table D.4-4, p90 of the application
QALY = quality-adjusted life year

The base case produced an incremental cost-effectiveness ratio (ICER) of $25,163 per QALY gained over the patient's lifetime. At a 3% discount rate, the ICER was $25,238 per QALY gained.

The application also presented the results of selected univariate sensitivity analyses.

Table 6: Univariate sensitivity analyses

Univariate analyses	Incremental costs	Incremental QALYs	ICERs
Base case	**$25,505**	**1.01**	**$25,163**
Transition probabilities	-	-	-
Baseline all-cause mortality estimate 10.2% per annum based on MAGGIC HF risk calculator	$22,886	1.29	$17,774
Relative risk for all-cause mortality Increased to 0.84 based on 17 month results from CHAMPION	$24,468	0.83	$29,407
Baseline HF-related hospitalisation estimate 32% per annum based on Robertson et al 2012	$28,039	1.01	$29,735
Relative risk for HF-related hospitalisation increased to 0.72 based on 17 month results from CHAMPION trial	$26,690	1.01	$26,333
Relative risk of all-cause mortality in the intervention arm set to 1.0 (i.e. no treatment effect compared to standard care) after 3 years	$23,308	0.63	$37,059
Relative risk of HF-related hospitalisation in the intervention arm set to 1.0 (i.e. no treatment effect compared to standard care) after 3 years	$30,961	1.01	$30,547
Utility values	-	-	-
Preference based quality of life weighting for survival removed (i.e. Cost per LY)	$25,505	0.91	$28,136
Utility weight set to parity in both arms at 0.711 (baseline utility)	$25,505	0.64	$39,572
Utility weight assumed to decline 5% per annum (i.e., 0.42% per month) after 17 months	$25,505	0.75	$34,085
Costs	-	-	-
Haemodynamic sensor device cost increased by 20%	$21,505	1.01	$21,217
Haemodynamic sensor device cost decreased by 20%	$29,505	1.01	$29,110
HF-related hospitalisation cost increased by 20%	$26,432	1.01	$24,249
HF-related hospitalisation cost decreased by 20%	$24,578	1.01	$26,078
Optimised medication costs for the intervention arm doubled	$24,258	1.01	$23,933
Optimised medication costs for the intervention arm halved	$27,998	1.01	$27,623
Monitoring costs for the intervention arm doubled	$25,109	1.01	$24,773
Monitoring costs for the intervention arm halved	$26,297	1.01	$25,944

The independent critique considered the ICER results to be "highly uncertain and likely to favour the intervention" because:

- The heart failure-related hospitalisation rate for the standard care arm (71.8%) might be overestimated;
- The elevated survival benefit for patients with the sensor, compared to the standard care patients, was inappropriate because there was no difference in overall survival between the two arms in the CHAMPION trial;
- Utility values were applied inappropriately as they are not associated with health states (such as heart failure, stable condition, complication) but with the cycle (advancing time);
- Device failure at implantation was not taken into account in the economic model and; and
- Anaesthesia and other relevant costs were not accounted for in the economic model.

The independent critique undertook the additional sensitivity analyses outlined in Table 7, and concluded that the model was not robust with respect to key variables and assumptions, and that the ICER presented in the application was highly uncertain and likely to be underestimated.

Table 7: Results of additional sensitivity analyses

Sensitivity analysis	Incremental costs	Incremental QALYs	Incremental cost-per QALY
Base case	**$25,505**	**1.01**	**$25,163**
Univariate sensitivity analysis	**-**	**-**	**-**
(A) Model duration: 10 years vs. base case = lifetime	$24,851	0.69	$36,070
(B) Implantation failure incorporated in device-related and system-related complication: (25+15)/575 vs. base case = 15/575	$26,062	1.01	$25,714
(C) Utility values assigned to health states: baseline: 0.711, stable HF = 0.78; hospitalisation = 0.57; vs. base case = utility assigned by cycle	$25,505	0.67	$37,913
(D) Revised probability of HF-related hospitalisation (8.5% in cycle 1 up to 30.5% in cycle 18+ vs. base case)	$28,597	1.01	$28,214
(E) Revised relative risk of mortality: 0.94 vs. base case = 0.79	$22,641	0.51	$44,198
Multivariate sensitivity analysis	**-**	**-**	**-**
(A) + (B)	$25,408	0.69	$36,880
(A) + (B) + (C)	$25,408	0.36	$69,780
(A) + (B) + (C) + (D)	$28,514	0.36	$79,111
(D) + (E)	$22,641	0.21	$105,645
(B) + (C) + (D) + (E)	$27,200	0.16	$171,315
(A) + (B) + (C) + (D) + (E)	$27,406	0.10	$276,859

Source: estimated during the evaluation
HF = heart failure; QALY = quality-adjusted life years

ESC had concerns with the economic model, which presented a different structure to the three proposed structures in the final Protocol. However, the applicant asserted that the utility values and economic approach used were the same as for MSAC application 1223 (insertion, replacement, or removal of a cardiac resynchronisation therapy device capable of defibrillation for mild, moderate or severe chronic heart failure). The application applied utility weights derived from the CHAMPION trial to the intervention and comparator arms over the model lifetime time horizon (assuming continuous utility gains of 0.079 for each cycle after 6 months (0.739-0.660), which led to an ICER in favour of the intervention. ESC suggested that the two models (from this application and Application 1223) be compared.

On further inspection of the model for this application, ESC also had concerns that the mortality rate was duplicated across both hospitalised and stable patient populations. The same mortality reduction rate was also used across the model. ESC again questioned the appropriateness of this methodology.

The critique of the application suggested that the economic model should have incorporated anaesthesia costs. However, ESC supported the applicant's statement that that sedation alone would be used for the majority of procedures

13. Financial/budgetary impacts

The application presented a financial analysis, which indicated that the cost to the MBS would "remain below $1m in Year 5".

Table 8: Net healthcare costs over 5 years

Description	2016	2017	2018	2019	2020
Number of patients treated with LAB-IHMS	48	168	384	672	960
Medical services cost	$38,972	$136,403	$311,777	$545,610	$779,443
Hospital services cost	$406,224	$1,421,784	$3,249,792	$5,687,136	$8,124,480
System components cost	$960,000	$3,360,000	$7,680,000	$13,440,000	$19,200,000
Net healthcare costs	$1,405,196	$4,918,187	$11,241,569	$19,672,746	$28,103,923
Net offsets from HF-related hospitalisations avoided	$92,061	$230,153	$414,276	$552,368	$552,368
Net healthcare costs with cost offsets	$1,313,135	$4,688,033	$10,827,293	$19,120,378	$27,551,555

The application estimated that 2,232 patients would receive the sensor in the first five years of listing on the MBS based on the estimated number of sites that could perform the surgery and the number of implants per month at each site. The independent critique considered that there was insufficient information or justification to determine whether these assumptions were reasonable. Table 9 provides the estimated number of services per year and net costs to MBS provided in the application.

Table 9: Estimated number of sensor implants provided per patient for Years 1 to 5 and the MBS costs

	Year 1	Year 2	Year 3	Year 4	Year 5
Number of services per year	48	168	384	672	960
Cost to MBS (proposed service)	$33,317	$116,611	$266,538	$466,442	$666,346
Cost of anaesthesia required for the implant	$5,655	$19,792	$45,239	$79,168	$113,098
Total net cost to the MBS	$38,972	$136,403	$311,777	$545,610	$779,443

Source: Table E.2-1, p94, Table E.4-2, p97 of the application
MBS = Medicare Benefits Schedule

From the evidence included in the application, ESC noted that 7% of implantation attempts were unsuccessful. The impact of this on the need for repeat procedures was not factored into the financial impacts or the economic evaluation.

14. Key issues from ESC for MSAC

ESC noted that a range of issues were raised in the critique. However, ESC considered that many of these were not highly relevant for decision making, and that others had been adequately addressed in the applicant's pre-ESC response. ESC considered that the key issues which should be considered by MSAC were:

- whether there is sufficient evidence of safety regarding adverse events of the implantation procedure – long-term safety and risk of device failure is unclear;
- the level and frequency of patient monitoring needed after the procedure should be specifically delineated;
- the applicability of supporting data to the target population is unclear (average patient age of 61 vs. 80); and
- there are economic model uncertainties, such as the duplication of the mortality rate and mortality reduction rate across the model, and rationale for attribution of utility states in the current models.

15. Other significant factors

Nil.

16. Applicant's comments on MSAC's Public Summary Document

St Jude Medical acknowledges MSAC's consideration of the proposed listing of Application 1398 – *Implantation of a permanent leadless and batteryless haemodynamic sensor and associated remote analysis of pulmonary artery pressure for patients with moderate chronic heart failure (New York Heart Association class III)*.We are reassured to note MSAC agreed that a clinical need for pulmonary artery pressure monitoring was established within the target patient population and there were no concerns with the clinical evidence supporting this therapy. The Applicant accepts minor alterations to the economic model are required to address residual areas of uncertainty. In deferring its advice for public funding, MSAC requested information related to the implementation of the proposed service be addressed. St Jude are committed to working with MSAC to provide this information noting the current clinical management algorithm for this patient group is complex and as a consequence there is considerable variability in standard care practices. St Jude Medical will continue to work with Australian clinicians and other stakeholders to address issues related to the implementation of pulmonary artery pressure monitoring into Australian clinical practice but would welcome any guidance offered by MSAC on how this can be achieved.

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website at: www.msac.gov.au