



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application 1374 – Insertion of subcutaneous electrode for the purpose of use with an implantable cardioverter defibrillator (ICD)

Applicant: Boston Scientific

Date of MSAC consideration: MSAC 62nd Meeting, 26 – 28 November 2014

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

An application requesting Medicare Benefits Schedule (MBS) listing for the insertion of a subcutaneous implantable cardioverter defibrillator (ICD) electrode was received from Boston Scientific by the Department of Health in September 2013.

2. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to safety, clinical effectiveness and cost-effectiveness, MSAC did not support public funding for the insertion of a subcutaneous implantable cardioverter defibrillator (S-ICD) electrode because of uncertain comparative long-term safety and clinical effectiveness which translated into uncertain cost-effectiveness.

MSAC considered that a prospective, multi-centre, randomised controlled trial (PRAETORIAN) comparing an S-ICD with a transvenous ICD (T-ICD) scheduled for completion in June 2018, may assist to address these uncertainties.

MSAC considered that any reapplication should be made via ESC and would require external evaluation.

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

MSAC noted that S-ICD therapy is an alternative option to T-ICD for patients that do not require pacing therapy and in whom insertion of a T-ICD is not ideal or feasible. Australian expert opinion estimates that 75-80% of current T-ICD patients could potentially receive S-ICD.

MSAC noted that the evidence base for evaluation of the comparative safety and effectiveness for S-ICD was limited and based on small, non-randomised, unblinded studies with short term follow-up and surrogate (largely technical) endpoints. MSAC noted that this limited evidence raised a number of uncertainties such as:

- levels of inappropriate shock (for short-term studies);
- effect of physical activity (especially contact sport);
- potential for increased complications with S-ICDs vs T-ICDs;
- effect of larger sized generator and position of subcutaneous electrode on patient discomfort levels;
- potential for T-wave over-sensing with S-ICDs;
- rates of lead migration/dislodgement;
- use of surrogate efficacy endpoints (technical performance and safety of ICD) in the absence of patient-relevant outcomes such as sudden cardiac death and overall death; and
- no health-related quality of life outcomes were provided.

Based on the evidence presented and the uncertainties listed above, MSAC was not convinced that the claim of S-ICD non-inferiority had been proven in terms of comparative safety and effectiveness. MSAC considered that the long-term safety of S-ICD was particularly uncertain due to the limited follow-up in the studies presented. MSAC suggested the results from a large prospective, multi-centre, randomised controlled trial (PRAETORIAN) due for completion in June 2018 may help to address the uncertainties.

MSAC questioned the ability of the current data set to address the assumption of non-inferior safety and clinical effectiveness and therefore considered that this uncertainty flowed on to the economic evaluation as the cost-minimisation analysis was presented based on an assumption of non-inferiority between the two ICD devices. Total health care costs were calculated at \$64,620 per S-ICD procedure and \$69,296 per T-ICD procedure, resulting in a cost saving of \$4,677 per procedure (decreasing to \$3,072 if a 1% pa conversion from S-ICD to T-ICD is assumed). It was noted that this estimation was reliant on the accuracy of the number of eligible patients and uptake of S-ICD in Australia.

MSAC was concerned that the assumptions for similar resource use for S-ICD compared to T-ICD may not be reasonable as S-ICD lead insertion is relatively straightforward and would take half the time of T-ICD. Therefore, the fee reduction may be too small in recognition of the simpler and shorter procedure time of S-ICD relative to T-ICD procedures. MSAC considered that, overall, the resources required for the implantation of S-ICD are similar to T-ICD in terms of staffing and infrastructure, although fluoroscopy is not required.

Sensitivity analyses on the uncertainties identified indicated that fewer cost savings for MBS would occur for listing S-ICD therapy if there was increased market growth, greater switching from S-ICD to T-ICD and X-ray costs were included.

MSAC identified other factors that also had the potential to impact on the economic modelling and increase financial uncertainty around this intervention such as:

- outcome data limited to under five years;
- overestimated proposed fee for S-ICD lead placement;
- underestimation of patients that will develop pacing requirements after S-ICD insertion; and
- reduced battery life due to higher defibrillation threshold.

4. Background

MSAC has not previously considered this application.

5. Prerequisites to implementation of any funding advice

There are S-ICD leads and generators currently listed in the Australian Register of Therapeutic Goods (ARTG).

The cost of the generator associated with S-ICD leads will separately require consideration for reimbursement through the Prostheses List.

Implantation of an S-ICD device is clinically similar to the insertion of a T-ICD in terms of staffing, and required infrastructure. As such, the necessary capabilities to perform S-ICD implantation are already established at the relevant clinics and institutions.

6. Proposal for public funding

There are existing MBS items for insertion of T-ICD leads in primary prevention (item 38384; Table 1) and secondary prevention (item 38390; Table 2). The associated MBS items for the insertion or replacement of an automatic defibrillator generator are items 38387 and 38393.

The proposed listing for the S-ICD lead is below.

Proposed MBS item descriptor for insertion, removal or replacement of subcutaneous ICD lead

Category 3 – Therapeutic Procedures
SUBCUTANEOUS DEFIBRILLATOR LEAD, insertion, removal or replacement of, for prevention of sudden cardiac death in patients who do not have symptomatic bradycardia, incessant ventricular tachycardia, or spontaneous, frequently occurring ventricular tachycardia that is reliably terminated with anti-tachycardia pacing. Multiple Services Rule (Anaes.) (Assist.) Fee: \$TBD

Specifically, S-ICD is only indicated for the treatment of life-threatening ventricular arrhythmias in patients who do not have symptomatic bradycardia, incessant VT, or spontaneous, frequently recurring VT that is reliably terminated with anti-tachycardia pacing.

Specialists involved in the insertion of a S-ICD lead would be the same with the proposed listing. As is the case for T-ICD lead insertion, all S-ICD lead insertions will take place in a hospital setting.

7. Summary of Public Consultation Feedback/Consumer Issues

Consumers noted that the item appears to offer a yet-to-be-proven default option for a small number of patients and that there is inadequate evidence, pending the 2018 study report. As a result, there is inadequate modelling based on inadequate evidence.

8. Proposed intervention's place in clinical management

The S-ICD comprises of an electrode and pulse generator. In contrast to traditional ICDs, this ICD is entirely subcutaneous. Accordingly, the system does not require an electrode to be

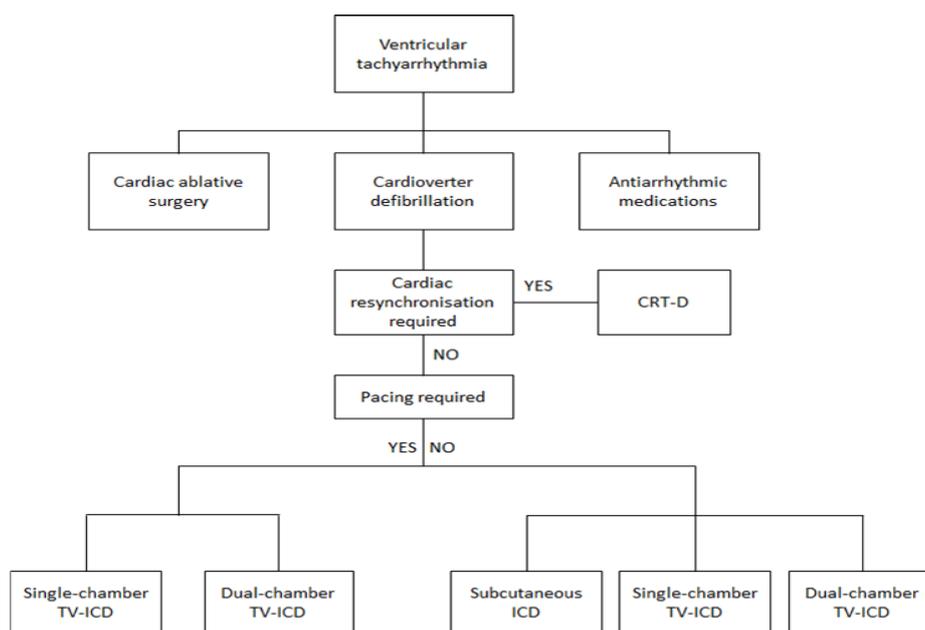
placed either on (epicardially) or in (endocardially) the heart and no leads are passed through the venous system. The implant procedure for the S-ICD involves making a pocket for the pulse generator in the lateral thoracic region. Using a tunnelling tool, the electrode is then placed in a subcutaneous sinus along the sternum. Using anatomical landmarks only, there is no need for fluoroscopy or other medical imaging during the surgical implant procedure. The electrode is connected to the pulse generator and the system then monitors cardiac rhythms, delivers defibrillation and/or post-shock bradycardia pacing therapies as required, and records ventricular tachyarrhythmia events for subsequent clinician review. A pre-procedure chest X-ray is usually performed and a post-procedure chest X-ray is used to check the position of the generator.

Currently, T-ICD devices are able to provide cardiac pacing to treat dangerously low heart rates (bradycardia), if present (eg. following appropriate shock). However, the majority of patients implanted with an ICD do not have a bradycardia pacing indication. Insertion of the S-ICD is clinically similar to the insertion of a T-ICD, yet the S-ICD leads do not need to be inserted into the vasculature of the heart. Rather, they are placed under the skin of the patients' chest.

The S-ICD is intended to provide defibrillation therapy for the treatment of life threatening ventricular tachyarrhythmias in patients who do not have symptomatic bradycardia, incessant ventricular tachycardia, or spontaneous, frequently recurring ventricular tachycardia that is reliably terminated with anti-tachycardia pacing.

It was claimed that the S-ICD system provides similar clinical benefits as T-ICDs while minimising the risk of some long-term complications associated with T-ICD lead failure. MSAC noted that the S-ICD system provides some of the clinical benefits of T-ICD i.e. it does not have the capacity to provide pacing.

Below is the proposed clinical management pathway for patients with ventricular arrhythmia at risk of sudden cardiac death.



9. Comparator

The application nominated single and dual-chamber T-ICD therapy as the comparator.

There are existing MBS listed items for T-ICD therapy. The comparator also provides anti-tachycardia pacing and bradycardia pacing support. The number of patients suitable for T-ICD therapy is greater than S-ICD therapy however, it is estimated that 75-80% of T-ICD patients would be suitable for S-ICD therapy. The insertion of the transvenous lead into the heart vasculature for treatment is more complicated than inserting a subcutaneous lead. It requires correct positioning, with higher procedural risk and greater demand on medical imaging. Another disadvantage of transvenous lead placement is the increased physical stress exhibited on the leads as a result of cardiac motion, and thus increased risk for lead fracture.

S-ICD has significant functional limitations as it cannot provide long-term bradycardia pacing or anti-tachycardia pacing. Nor does S-ICD have remote monitoring capability – a feature that decreases the number of scheduled clinic-based device checks and may improve patient outcomes and simplifies follow-up (Aziz et al 2014).

The physical size of the S-ICD generator is 30 percent larger than the T-ICD generator. Expert opinion advised that, once “well healed in”, this should not result in significant discomfort and no worse than for T-ICD. The S-ICD system energy requirements are greater than T-ICD therapy, due to the reduced proximity of S-ICD lead to the heart. Due to the higher energy demand, the battery life of the S-ICD generator is shorter (~5 years) than the T-ICD generator (~10 years).

10. Comparative safety

The evidence presented in the SBA included three comparative studies (Köbe, 2013, Jarman 2012, Pettit 2013), five non-comparative studies (Dabiri Abkenari, 2011, Aydin, 2012, IDE Study, Olde Nordkamp, 2012, Kooiman, 2013), one study consisting of comparative and non-comparative sub-studies (Bardy, 2010) and one registry trial (EFFORTLESS; Lambiase, 2014).

The SBA presented data on a range of safety outcomes including device-related complications and adverse events (including infection).

The evaluation considered that overall, the clinical evidence was insufficient to assess the long-term safety of subcutaneous ICD therapy. This was largely due to absence of a randomised controlled trial and small sample sizes with short follow-up durations to observe lifelong treatment anticipated with these patients. Of particular concern was the lack of sub-group analysis of younger patients who represent an additional population if MBS listed.

11. Comparative effectiveness

The SBA presented surrogate efficacy endpoints for the technical performance and safety of the ICDs in the absence of patient-relevant outcomes such as sudden cardiac death and overall death. The four main efficacy (device-related) outcomes were ‘successful conversion tests’, ventricular fibrillation or tachycardia appropriately detected and successfully treated, and ‘patients with inappropriate shocks’. The primary analysis of non-inferiority was based on observational case control and cohort studies, single arm studies and registry results.

No health-related quality of life outcomes were provided; the evaluation noted that these should be available with completion of a large blinded randomised controlled trial in 2018.

The table below summarises the key study results; meta-analysis was performed by the applicant when possible.

Summary of the key evidence -comparative studies for primary analysis

Outcome	Köbe 2013		Jarman 2012		Pettit 2013		Meta-analysis	
	S-ICD	TV-ICD	S-ICD	TV-ICD	S-ICD	TV-ICD	S-ICD	TV-ICD
Successful conversion tests ^a (%)	60/67 (89.5)	59/65 (90.8)	16/16 (100)	NR	NR	NR	<i>Not calculable</i>	
	RR=0.99 (0.88, 1.10) P=0.81		N/A		N/A			
VT or VF episodes appropriately detected (%)	3/3 (100)	9/9 (100)	8/8 (100)	3/3 (100)	3/3 (100)	1/1 (100)	14/14 (100)	13/13 (100)
	P=1.00		P=1.00		P=1.00		RR=1.00 (0.76, 1.31) P=1.00	
VT or VF episodes successfully treated (%)	3/3 (100)	NR	8/8 (100)	NR	3/3 (100)	1/1 (100)	<i>Not calculable</i>	
	N/A		N/A		P=1.00			
Patients experiencing inappropriate shocks (%)	3/69 (4.3)	3/69 (4.3)	4/16 (25)	1/16 (6.3)	1/9 (11.1)	3/6 (50)	8/94 (8.5)	7/91 (7.7)
	P=1.00		P=0.19		P=0.14		RR=0.95 (0.21, 4.27) P=0.95	
Complications requiring surgical correction/hospitalisation ^b (%)	3/69 (4.3)	4/69 (5.8)	3/16 (18.8)	1/16 (6.3)	0/9 (0)	4/6 (66.7)	6/94 (6.4)	9/91 (9.9)
	P=0.70		P=0.32		P=0.07		RR=0.67 (0.12, 3.86) P=0.66	
Local or systematic Infection (%)	1/69 (1.4)	1/69 (1.4)	NR	NR	0/9 (0)	1/6 (16.7)	1/78 (1.3)	2/75 (2.7)
	P=1.00		N/A		P=0.35		RR=0.52 (0.07, 4.02) P=0.53	

Source: Table 38, p73 of the application

ICD = implantable cardioverter-defibrillator; NA = not applicable; NR = not reported; RR = relative risk; S = subcutaneous; TV = transvenous; VF = ventricular fibrillation; VT = ventricular tachycardia

a Successful conversion tests: An immediate intraoperative outcome to determine defibrillation ability of subcutaneous ICD device by terminating patient-induced ventricular fibrillation (sensitivity);

b Device-related complications: any adverse event related to specific ICD (ie. Hospitalisation events, explanation because of developed pacing needs or lead fracture, migration etc.)

The results reveal small and non-significant differences between the study arms for nearly all outcomes (especially in the largest comparative study by Köbe 2013). All relative risks were close to or less than 1.0 and in favour of subcutaneous ICD and none were statistically significant. Minimally important differences for these outcomes were not considered.

A supplementary analysis of single-arm studies is provided in the table below. As these studies were typically longer in duration, survival of patients with subcutaneous ICD could be observed; including 'deaths over a 12 month period'.

Summary of the main outcomes- single-arm subcutaneous ICD studies

Outcome	Bardy, 2010 c) LT study	Bardy, 2010 d) European trial	Aydin 2012	Dabiri Abkenari 2011	IDE trial	Olde Nordkamp 2012	Kooiman 2013	EFFORTLESS registry
Successful conversion tests (%)	6/6 (100)	52/53 (98)	39/40 (97.5)	31/31 (100)	304/304 (100)	118/118 (100)	NR	NR
VT or VF episodes appropriately detected (%)	NR	12/12 (100)	21/21 (100)	13/13 (100)	38/38 (100)	45/45 (100)	NR	NR
VT or VF episodes successfully treated (%)	NR	100	96.4	100	100	100	NR	93/93 (100)
Deaths per 12 months follow up (%)	NR	7.3	0	3.9	2.9	0	NR	4.6 ^a
Patients experiencing inappropriate shocks (%)	NR	0	7.50	10.3	8.5	8.5	9.1	1.3
Complications requiring surgical correction/hospitalisation (%)	NR	4/53 (7.3)	5/40 (12.5)	3/31 (9.7)	4/304 (1.2)	16/118 (14)	3/69 (4.3)	29/456 (6.4)
Infection (%)	NR	2/53 (3.6)	0	1/31 (3.2)	18/304 (5.6)	7/118 (5.9) ^b	NR	18/456 (3.9)

Source: Table 18, Appendix A of the application

LT = long term; NR = not reported; VF = ventricular fibrillation; VT = ventricular tachycardia

a Annual rate calculated based on mean follow-up of 558 days i.e. $(32 \div 558/365)/456$

b Type of lead complication not clear – only reported that revision was required in 2 patients

The SBA claimed the following therapeutic conclusions for S-ICD versus T-ICD treatments:

- S-ICD is non-inferior to T-ICD in terms of clinical efficacy; and
- S-ICD is non-inferior to T-ICD in terms of safety.

The evaluation considered the claims of ‘non-inferiority’ in regards to clinical efficacy and safety have several weaknesses including:

- Technical device-related outcomes were used as a ‘proxy’ to patient relevant outcomes. No attempt was made to correlate the surrogate outcomes with clinically relevant outcomes such as sudden cardiac death, all-cause death, health-related quality of life;
- As acknowledged by the applicant, all studies presented have a high risk of bias as they involved: non-randomised populations; high potential for selection bias, small sample sizes; insufficient study durations; insufficient numbers of clinical events for comparison of primary outcomes, descriptive statistical analyses only and heterogeneity between the samples;
- There are well-known safety risks associated with subcutaneous ICD therapy with patients receiving inappropriate shocks, infections and complications requiring re-surgery; and
- Outcomes are unclear in the sub-group of patients expected to benefit most from subcutaneous ICD, preferential ‘younger’ patients.

A large, prospective, multi-centre, randomised controlled trial (PRAETORIAN, target n=850) comparing S-ICD with T-ICD will be completed in June 2018; it may offer outcomes on sudden cardiac death, all cause deaths, health related quality-of-life over 30 months in addition to device-related outcomes.

Pre-modelling studies:

The application provided no pre-modelling studies for the cost-minimisation analysis. The applicability of the included studies to the Australian population may be a concern, due to the lack of Australian study data.

12. Economic evaluation

The SBA presented a cost-minimisation analysis. The SBA stated that subcutaneous and transvenous ICD are identical in terms of hospital setting, procedural time (one hour total), clinical expertise (no additional training), existing infrastructure and patient before and after care.

The evaluation considered that the assumptions for similar resource use may not be reasonable because the S-ICD lead insertion is relatively straightforward; estimated 5-10 minutes after prepping and draping the site, the electrode is tunnelled subcutaneously (access to a vein is not required), there is no need for fluoroscopy and no time needed to locate the best position in the atrium or ventricle. The implantation of the actual device would be similar to implanting a permanent cardiac pacemaker or T-ICD generator. Based on expert advice, the S-ICD procedure would take less than 30 minutes (half the time of T-ICD).

The table below summarises the results of the economic evaluation of the proposed intervention.

Total healthcare costs associated with S-ICD and TV-ICD

Resource Item ^a	Subcutaneous ICD	Transvenous ICD	Difference
MBS-related costs	-	-	-
MBS fee for ICD lead placement (For TV-ICD MBS #38384 or 38390 & 10% less for S-ICD)	\$947.39	\$1,052.65	-\$105.26
MBS fee for ICD generator insertion MBS # 38387 or #38393 (\$287.85 * 25% MSR)	\$71.96	\$71.96	\$0.00
Plain film imaging X-ray MBS # 58503 ^b	\$47.17 ^c	-	\$47.17
Anaesthetist service MBS # 21941	\$138.60	\$138.60	\$0.00
Anaesthetist service time units	\$39.60 (1/2 hour) (MBS # 23022,23031)	\$79.20 (1 hour) (MBS # 23043)	-\$39.60
Follow-up testing MBS # 38213(\$408.70 * 50% MSR)	\$204.35	\$204.35	\$0.00
Fluoroscopy MBS # 61109	-	\$258.90 ^c	-\$258.90
Non-MBS-related costs	-	-	-
Prostheses list fee for ICD leads ^d	\$4,680.00	\$9,000.00 ^e	-\$4,320.00
Prostheses list fee for ICD generator ^d	\$42,640.00	\$42,640.00	\$0.00
Hospitalisation costs ^f	\$15,850.66	\$15,850.66	\$0.00
Total health care costs per procedure	\$64,619.73	\$69,296.32	-\$4,676.59
Total additional cost of switching from S-ICD to a TV-ICD if pacing required	-	-	\$1,604.81 ^g
Net cost with pacing requirements	-	-	-\$3071.78^h

Source: Table 42, p79 of the application. *Corrections/additions made during evaluation.*

ICD = implantable cardioverter-defibrillator; MBS = Medicare Benefits Schedule; MSR = multiple services rule; S = subcutaneous; TV = transvenous

a Fees are provided at 100% schedule fee, no weighted average necessary for economic model

b MBS 58500 may also be used for chest X-ray

c Bulk Billing incentive applies for out of hospital services (schedule fee reduced by 5% and rebates paid at 100%)

d ARTG item 132315,128625 for S-ICD leads, item 142175 or 43 others for TV-ICD leads, item #219499 for S-ICD generator, item #154057 for single chamber TV-ICD generators (119 others at various prices)

e Total costs is for 1 unit device irrespective of single or dual chamber/leads

f Total hospitalisation cost calculated as the National Weighted Average Unit for implantation or replacement of an automatic ICD (3.1657), multiplied by the National Efficient Price for 2014-2015 (\$5,007)

g The explanation for this calculation is in Table D(i).2.2

h Total cost difference between subcutaneous ICD and transvenous ICD allowing for 1% switching

The economic evaluation excluded anaesthetist time units for both groups and chest X-ray potentially given to patients during subcutaneous ICD implantation pre- or post-procedurally (MBS item #58503). The proposed cost-savings changed slightly. Implantation of the S-ICD system was estimated to be cost saving by an estimated \$4,677 per procedure. The cost-savings to the MBS are driven by the proposed 10% reduced lead insertion fee and the removal of medical imaging requirements (fluoroscopy). This fee reduction may be too small in recognition of the simpler and shorter procedure time of S-ICD relative to T-ICD procedures.

13. Financial/budgetary impacts

The financial impact of the MBS listing to the Government estimates cost-savings to the MBS of \$25,232 in 2015, increasing to \$63,259 over five years (see table below). The estimates are driven by the cost offsets to the MBS from fewer fluoroscopies required for subcutaneous ICD lead insertion.

Net financial implications for the MBS

Variable	2015	2016	2017	2018	2019
Substitution of TV-ICD lead procedures by S-ICD (number)	121	162	206	253	303
Additional S-ICD use in patients unsuitable for TV-ICD	6	8	10	13	16
Total S-ICD procedures	127	170	216	266	319
Cost of S-ICD lead placement	\$122,996	\$164,515	\$209,249	\$257,197	\$308,359
Cost of patients switching to TV-ICD	\$1,970	\$2,635	\$3,351	\$4,119	\$4,939
Total cost of S-ICD	\$124,966	\$167,150	\$212,600	\$261,316	\$313,298
Total estimated cost offsets from substitution of TV-ICD	\$150,199	\$200,900	\$255,527	\$314,079	\$376,557
Total cost of S-ICD lead insertion to the MBS (savings)	-\$25,232	-\$33,750	-\$42,927	-\$52,763	-\$63,259

Source: Table 63, p109 of the application

ICD = implantable cardioverter-defibrillator; MBS = Medicare Benefits Schedule; S = subcutaneous; TV = transvenous

The evaluation considered the estimation is uncertain and relies on the accuracy of the number of eligible patients and uptake of S-ICD in Australia. Patients who currently have a contraindication to T-ICD may be eligible for S-ICD.

Sensitivity analyses were not provided in the application. A number of uncertainties were identified during evaluation and sensitivity analyses were undertaken. The table below summarises the results of the sensitivity analysis conducted during the evaluation.

Sensitivity analysis of the estimated net cost to the MBS

Variables for One-way Sensitivity Analysis/Year	2015	2016	2017	2018	2019
Overall net cost base case	-\$25,232	-\$33,750	-\$42,927	-\$52,763	-\$63,259
% TV-ICD popn eligible for S-ICD (75% base case)	-	-	-	-	-
Low estimate (70%)	-\$23,550	-\$31,500	-\$40,065	-\$49,245	-\$59,041
High estimate (80%)	-\$26,914	-\$36,000	-\$45,788	-\$56,280	-\$67,476
Growth due to additional patient popn (5% base case)	-	-	-	-	-
Estimate (10%)	-\$19,375	-\$25,916	-\$32,962	-\$40,515	-\$48,575
Estimate (20%)	-\$7,661	-\$10,247	-\$13,034	-\$16,021	-\$19,207
Uptake rates (<55 years = 5-15%, >55 years = 2-10%) ^a	-	-	-	-	-
Low estimate (<55 0%-10%, >55 0% - 5%)	-\$1,332	-\$7,784	-\$19,290	-\$27,069	-\$35,035
High estimate (<55 10% -20%, >55 10% -15%)	-\$49,133	-\$57,747	-\$71,415	-\$81,355	-\$91,483
Switching to TV-ICD - pacing needed (1% base case):	-	-	-	-	-
Estimate (7%)	-\$13,413	-\$17,940	-\$22,819	-\$28,047	-\$33,627

<i>Variables for One-way Sensitivity Analysis/Year</i>	<i>2015</i>	<i>2016</i>	<i>2017</i>	<i>2018</i>	<i>2019</i>
<i>Estimate (10%)</i>	<i>-\$7,503</i>	<i>-\$10,036</i>	<i>-\$12,765</i>	<i>-\$15,689</i>	<i>-\$18,810</i>
<i>Proposed fee (less 10% of TV-ICD: base case = \$947.39)</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>
<i>Lower proposed fee (less 20%= \$842.12)x75%MBS</i>	<i>-\$35,314</i>	<i>-\$47,235</i>	<i>-\$60,079</i>	<i>-\$73,846</i>	<i>-\$88,535</i>
<i>Lower proposed fee (less 50%= \$526.33) x75%MBS</i>	<i>-\$65,559</i>	<i>-\$87,690</i>	<i>-\$111,533</i>	<i>-\$137,090</i>	<i>-\$164,361</i>
<i>Include chest X-ray SC-ICD & anaesthetist time units</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>
<i>Other MBS fees</i>	<i>-\$24,151</i>	<i>-\$32,304</i>	<i>-\$41,087</i>	<i>-\$50,502</i>	<i>-\$60,548</i>
<i>Revised Scenario (Multi-way Sensitivity Analysis)</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>	<i>-</i>
<i>(10% growth; 7% pacing and chest X-ray & anaesthetist time)</i>	<i>-\$6,081</i>	<i>-\$8,133</i>	<i>-\$10,345</i>	<i>-\$12,716</i>	<i>-\$15,245</i>

Source: calculated during evaluation

ICD = implantable cardioverter-defibrillator; MBS = Medicare Benefits Schedule; S = subcutaneous; TV = transvenous; a Uptake rate in incident cases.

The financial sensitivity analyses indicated:

- The proposed fee for the subcutaneous lead insertion was the most influential value in the financial estimates. The lower the fee, the higher the cost savings for the MBS however this may keep uptake low in favour of the higher fee incentive for T-ICD;
- Increased uptake rates will save MBS costs, due to the cheaper subcutaneous ICD lead service fee than T-ICD;
- Fewer cost savings to MBS will occur if expected market growth was greater;
- Increased switching rates resulted in a reduction in MBS cost saving for listing subcutaneous ICD and substantial increases in public hospital costs would be expected;
- Fewer cost savings for MBS would occur for listing S-ICD therapy if there was increased market growth, greater switching from T-ICD and X-ray costs were included.

14. Key issues from ESC for MSAC

ESC noted a key issue for MSAC consideration would be the appropriateness of not including detailed patient inclusion criteria in the proposed MBS item descriptor for S-ICD lead service provision (in contrast to T-ICD MBS item descriptors).

ESC agreed the descriptor needs to be:

- Explicit, particularly for primary prevention
- Guideline-based
- Specific to include: -
 - Patients with left ventricular ejection fraction (LVEF) of $\leq 30\%$ at least one month after myocardial infarction when the patient has received optimal medical therapy; and
 - Patients with chronic heart failure associated with mild to moderate symptoms (New York Heart Association II and III) and LVEF $\leq 35\%$ when the patient has received optimal medical therapy.
- Specific regarding exclusion criteria eg need for either bradyarrhythmia pacing or tachycardia overdrive pacing (eg. VT < 170 beats/min).

ESC expressed concerns about the patient experience with the S-ICD versus the T-ICD, namely the size and location of the implanted pulse generator and the intensity of the shocks.

ESC noted that the non-inferiority claim is questionable based on the clinical evidence which shows that the:

- Level of inappropriate shocks is quite high for these largely short-term studies. This may be reflective of the limitation of subcutaneous ICD system in regards to ‘T-wave oversensing’. Clinical evidence reports that children make up 25% of the patients associated with these subcutaneous ICD inappropriate shocks (Köbe 2013) and that quality of life is adversely impacted with these events (not reported in application).
- Complications and infection rates between the subcutaneous and transvenous ICD are unclear based on the evidence presented in the presence of: heterogeneity, small sample sizes, confounding variables not appropriately controlled for and differential follow-up across treatment with S-ICD compared to control group with T-ICD therapy (Pettit 2013). Like the surrogate technical outcomes, the safety outcomes do not report sample size calculations and events were underpowered for comparison. All reported confidence intervals for outcomes are much wider for safety outcomes, highlighting the greater levels of uncertainty.

ESC noted the uncertainty on whether S-ICD is non-inferior to T-ICD in terms of its safety profile. Evidence was variable and inconclusive. The critique noted the issue of the electrode being close to the pectoral muscles where chest muscle activity can be over-sensed or miss-sensed as irregular ventricular activity is not adequately addressed.

ESC expressed concerns around false positive and false negative incidences with S-ICD. The concerns ESC had regarding over-sensing may be offset in the future by developments in programming.

ESC noted there is a paucity of clinical trial data:

- All evidence presented in the application is based on non-randomised studies and only device-related/technical and safety outcomes were assessed;
- As a whole, the sample sizes were all very small in the primary analyses, especially in Jarman (2012) and Pettit (2013) which had 16 and 9 patients in the treatment arms, respectively;
- This reduces the generalisability of the findings to the intended MBS population;
- A prospective, multi-centre, randomised controlled trial (PRAETORIAN) comparing subcutaneous ICD with transvenous ICD will be completed in June 2018; and
- No health-related quality of life data are yet available.

Compared with S-ICD, T-ICD therapy is susceptible to:

- Greater surgical complications (as a result of lead failure and infection);
- Greater severity of any infection due to connection with heart and greater vasculature;
- Greater complexity in lead removal, which is especially important in eligible younger patients;
- Endovascular mechanical stress producing lead malfunction and failure (Aziz et al. 2014); and
- Greater associated- mortality and morbidity in patients with chronically present transvenous leads.

Subcutaneous ICD does not have remote monitoring capability – a feature that decreases the number of scheduled clinic-based device checks, may improve patient outcomes, and simplifies follow-up (Aziz et al 2014).

There is uncertainty around the potential setting for subcutaneous ICD and the credentialing of health professionals required for this less invasive procedure compared with conventional ICD implantation.

ESC was concerned that the proposed fee may not be justified. The proposed fee is 10% less than for transvenous ICD. However, expert opinion indicates that the complexity and time required for implantation are closer to 50% of that required for transvenous ICD. The appropriateness of the proposed fee for implantation of a subcutaneous ICD, based on '10% less' (than transvenous ICD) which may reflect an overestimate of the cost of the procedure that is less invasive, simpler and quicker than transvenous ICD.

ESC agreed the main areas of financial uncertainty relate to:

- The lack of supportive data collection beyond the five year financial model, where key device revision and replacement is expected to occur, and the long-term economic implications to the Australian healthcare system. The limited experience and follow-up of subcutaneous ICD in practice which significantly reduces the ability to forecast all economic costs, especially beyond five years where re-implantation and the associated safety risks may occur;
- The appropriateness of assumptions used to estimate the 'additional' patient group; calculations show that if the growth is higher than 5% the saving to the MBS will be significantly reduced;
- The estimation of the number of subcutaneous ICD patients who then require transvenous ICD as a result of developing pacing requirements. HESP advised that the 'broader' population base proposed would be in the order of 10-20% switching rate, significantly reducing the savings to MBS;
- The appropriateness of assumptions used to identify and estimate the eligible patients for subcutaneous ICD; calculations show greater numbers of patients eligible will generate greater cost savings to the MBS;
- The uncertainty regarding the assumed gradual growth of subcutaneous ICD uptake rates (based on historical MBS transvenous ICD service provision). Review of AIHW and other external data sources indicate this growth could be rapid and exponential; and
- The unknown applicability to the proposed Australian population because no study included Australian patients.

15. Other significant factors

Nil

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

Boston Scientific are disappointed with MSAC's decision not to recommend the insertion of a subcutaneous implantable cardioverter defibrillator (S-ICD) electrode in Australia. The evidence presented in this submission supports the technical equivalence of S-ICD and TV-ICD in the proposed patient population, with the benefit of fewer surgical complications and lesser severity of infection. Boston Scientific understands MSAC's suggestion to wait for long-term, patient-relevant outcomes, but believe the current body of evidence sufficiently justifies funding pending additional evidence. The PRAETORIAN trial will likely address some, but not necessarily all of MSAC's concerns and will not be available for up to four years, so other funding options may be considered pending this additional evidence.

The Sponsor will continue to work with Australian physicians and other stakeholders to secure access for patients to address the unmet clinical need for S-ICD within the current ICD population. Notably, S-ICD has been approved in United Kingdom, where NICE have conditionally agreed to reimburse the technology for eligible patients, with further collection of data. Boston Scientific are committed to working with MSAC and the Department of

Health to ensure the health outcomes of Australian patients at risk of sudden cardiac death do not fall behind those of comparable nations.

17. Further information on MSAC

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