



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application 1223 – Insertion, replacement or removal of a cardiac resynchronisation therapy device capable of defibrillation (CRT-D) for mild chronic heart failure

Sponsor/Applicant/s: Optum Insight

Date of MSAC Meeting 28 November 2013

1. Purpose of application

An application requesting amendments to existing Medical Benefits Schedule (MBS) items for the insertion, replacement, or removal of a cardiac resynchronisation therapy device capable of defibrillation (CRT-D) and associated leads, to include patients with mild chronic heart failure, was received from Optum (working with Biotronik, Boston Scientific, Medtronic and St. Jude Medical) by the Department of Health in May 2012.

CRT-D implantation involves insertion of a generator in the upper chest, with placement of three electrode leads that connect the generator to the heart. The right atrial lead is used for sensing and pacing; the right ventricular lead is used for sensing, pacing, defibrillation and/or cardioversion; and the left ventricular lead is used for cardiac resynchronisation. All three leads are inserted into the heart via the subclavian vein (or the cephalic or internal jugular vein in some cases). Specialised techniques are required to thread the left ventricular lead through the coronary sinus, and correctly position this lead inside a coronary vein.

The submission indicated that the specific medical services for the proposed intervention are the same as those currently used for insertion, removal, or replacement of a CRT-D device in patients with New York Heart Association (NYHA) class III or IV heart failure.

Ordinarily, CRT-D generators are replaced when the battery is exhausted, or at the clinicians discretion. Current implanted device batteries typically last between 5 and 8 years.

The proposed intervention is an extension of the services currently used for the insertion, removal, or replacement of a CRT-D device in patients with moderate to severe chronic heart failure (NYHA class III or IV) (MBS items 38371, 38368, 38654 and 38350).

Heart failure is a complex syndrome resulting from any structural or functional cardiac abnormality that reduces the ability of the heart to function as a pump (Cowie & Zaphiriou 2002) and is a major cause of morbidity and mortality in Western societies. The most

common cause of heart failure in the developed world is coronary heart disease with hypertension often a co-existing risk factor (Fox et al 2001). Many patients may have also suffered a previous myocardial infarction.

Patients may have heart failure with a preserved ejection fraction (HFpEF) or a reduced ejection fraction (HFrEF) (NICE 2010a). In some of these patients the left ventricle fails to pump in synchrony with the right ventricle (interventricular dyssynchrony) or the wall of the left ventricle may contract at different times (intraventricular dyssynchrony). The final Decision Analytic Protocol (DAP) focused on patients with HFrEF who have ventricular dyssynchrony.

The impact of the symptoms of heart failure on functional capacity can be assessed using the NYHA classification (Table 1 whereby subjective symptoms are used to group patients into one of four classes.

Table 1: NYHA classification of functional class for heart failure (NHF/CSANZ, 2011)

Class I	No limitations. Ordinary physical activity does not cause undue fatigue, dyspnoea or palpitations (asymptomatic left ventricular dysfunction).
Class II	Slight limitation of physical activity. Ordinary physical activity results in fatigue, palpitations, dyspnoea or angina pectoris (mild chronic heart failure).
Class III	Marked limitation of physical activity. Less than ordinary physical activity leads to symptoms (moderate chronic heart failure).
Class IV	Unable to carry on any physical activity without discomfort. Symptoms of CHF present at rest (severe chronic heart failure).

The submission proposed to expand the current MBS listing for CRT-D to include patients with mild chronic heart failure (NYHA class II) who are managed with optimal medical therapy (OMT) and meet the following criteria:

- sinus rhythm;
- left ventricular ejection fraction (LVEF) less than or equal to 30%; and
- QRS duration greater than or equal to 150 ms.

This patient population is currently eligible for implantable cardioverter defibrillator (ICD) therapy. The current application seeks to extend this to CRT-D therapy in those patients who meet the criteria listed above. Such technologies (ICD or CRT-D) are used in two main patient populations:

- As primary prevention in patients with low LVEF and who are at increased risk of cardiac arrest;
- As secondary prevention in patients with low LVEF and who have already suffered a cardiac arrest.

2. Background

In August 2005, MSAC Application 1042 reported on cardiac resynchronisation therapy (CRT) for severe heart failure. This report excluded CRT with an implantable defibrillator but included evidence from the Companion trial which compared CRT with CRT-D¹.

¹ Bristow, M. R., et al. (2004) 'Cardiac-resynchronization therapy with or without an implantable defibrillator in advanced chronic heart failure', *New England Journal of Medicine*, 350(21), 2140-2150.

In March 2006, MSAC Reference 32 reported on ICD for prevention of sudden cardiac death. This report included ICD with CRT capability based on the Companion trial.

Clinical input to the Protocol Advisory Sub-Committee (PASC) advised that it was appropriate for all current CRT-D devices to be grouped together for the purposes of the assessment.

3. Prerequisites to implementation of any funding advice

The implantable CRT-D devices are listed on the Australian Register of Therapeutic Goods (ARTG) to detect and treat tachyarrhythmias and for the treatment of heart failure through CRT. The associated leads are also listed on the ARTG.

4. Proposal for public funding

The proposed MBS item descriptors for the insertion, removal or replacement of a CRT-D generator and left ventricular electrode lead are shown below.

Applicant Proposed MBS item descriptor for 38371 (CRT-D device)

Category 3 – Therapeutic procedures
<p>MBS 38371 (proposed) PERMANENT CARDIAC SYNCHRONISATION DEVICE CAPABLE OF DEFIBRILLATION, insertion, removal or replacement of, for patients who have moderate to severe chronic heart failure (NYHA class III or IV) despite optimised medical therapy and who meet all of the following criteria:</p> <ul style="list-style-type: none"> – sinus rhythm – a left ventricular ejection fraction of less than or equal to 35% – a QRS duration greater than or equal to 120 ms. <p>And for patients who have mild chronic heart failure (NYHA class II) despite optimised medical therapy and who meet all of the following criteria:</p> <ul style="list-style-type: none"> – sinus rhythm – a left ventricular ejection fraction of less than or equal to 30% – a QRS duration greater than or equal to 150 ms. (Anaes.) <p>Fee: \$287.85 Benefit: 75% = \$215.90 85% = \$244.70</p>

Source: SBA p5, Table A-2

Applicant Proposed MBS item descriptor for 38368 (left ventricular lead via the coronary sinus)

Category 3 – Therapeutic procedures
<p>MBS 38368 (proposed) PERMANENT TRANSVENOUS LEFT VENTRICULAR ELECTRODE, insertion, removal or replacement of through the coronary sinus, for the purpose of cardiac resynchronisation therapy, for patients who have moderate to severe chronic heart failure (NYHA class III or IV) despite optimised medical therapy and who meet the following criteria:</p> <ul style="list-style-type: none"> – sinus rhythm – a left ventricular ejection fraction of less than or equal to 35% – a QRS duration greater than or equal to 120 ms. <p>And for patients who have mild chronic heart failure (NYHA class II) despite optimised medical therapy and who meet all of the following criteria:</p> <ul style="list-style-type: none"> – sinus rhythm – a left ventricular ejection fraction of less than or equal to 30% – a QRS duration greater than or equal to 150 ms. <p>Where the service includes right heart catheterisation and any associated venogram of left ventricular veins. Not being a service associated with a service to which item numbers 38200 and 35200 apply. (Anaes.)</p> <p>Fee: \$1224.60 Benefit: 75% = \$918.45</p>

Source: SBA p6, Table A-4

Applicant Proposed MBS item descriptor for 38654 (left ventricular lead via open thoracotomy)

Category 3 – Therapeutic procedures

MBS 38654 (proposed)

PERMANENT LEFT VENTRICULAR ELECTRODE, insertion, removal or replacement of via open thoracotomy, for the purpose of cardiac resynchronisation therapy, for patients who have moderate to severe chronic heart failure (NYHA class III or IV) despite optimised medical therapy and who meet the following criteria:

- Sinus rhythm
- A left ventricular ejection fraction of less than or equal to 35%
- A QRS duration greater than or equal to 120 ms.

And for patients who have mild chronic heart failure (NYHA class II) despite optimised medical therapy and who meet all of the following criteria:

sinus rhythm

a left ventricular ejection fraction of less than or equal to 30%

a QRS duration greater than or equal to 150 ms.

Where the service includes right heart catheterisation and any associated venogram of left ventricular veins. Not being a service associated with a service to which item numbers 38200 and 35200 apply. (Anaes.) (Assist.)

Fee: \$1224.60 **Benefit:** 75% = \$918.45

Source: SBA p7, Table A-6

The submission stated that no amendments would be required to the current MBS listings for the insertion of the right atrial and right ventricular leads as these procedures are currently funded for patients in the proposed MBS population.

The proposed eligibility for CRT-D implantation in NYHA II patients requires measurement of LVEF and QRS duration and determining the presence of sinus rhythm. The submission stated that these assessments are already part of standard practice for the assessment of chronic heart failure patients.

The proposed restriction for the listing of CRT-D in NYHA II patients who have not responded to optimal medical therapy prevents the potential for inappropriate treatment of a previously sub-optimally treated condition.

The submission stated that the insertion, removal, or replacement of a CRT-D in patients with NYHA class II heart failure will be performed by a specialist including cardiac surgeons, cardiologists or electrophysiologists. This is consistent with the current MBS listing for CRT-D in patients with NYHA class III and IV heart failure which does not limit the insertion, removal, or replacement of the device to cardiologists only. The proposed intervention is not expected to lead to any incremental training requirements.

5. Consumer Impact Statement

The Electrophysiology (EP) and Pacing Council of the Cardiac Society of Australia and New Zealand (CSANZ) supported changing the MBS descriptor for CRT-D to include NYHA Class II with QRS >150ms and LVEF <30% (although argued that it should be extended to <35%).

In regards to the comparator, the CSANZ considered that ICD is the appropriate comparator and that CRT pacing (CRT-P) therapy in this cohort of patients lacks evidence compared to both ICD and CRT-D.

The CSANZ would also support consideration of CRT-D insertion in patients with atrial fibrillation as long as they fulfilled the other criteria for CRT-D.

6. Proposed intervention's place in clinical management

The submission suggested that a proportion of NYHA class II patients currently receiving ICD would instead receive CRT-D if it were reimbursed. An MBS benefit is available to NYHA class II patients for the insertion of an ICD device (item 38387). In the base case financial analysis of the submission it was estimated that 20% of patients receiving MBS item 38387 would instead receive CRT-D.

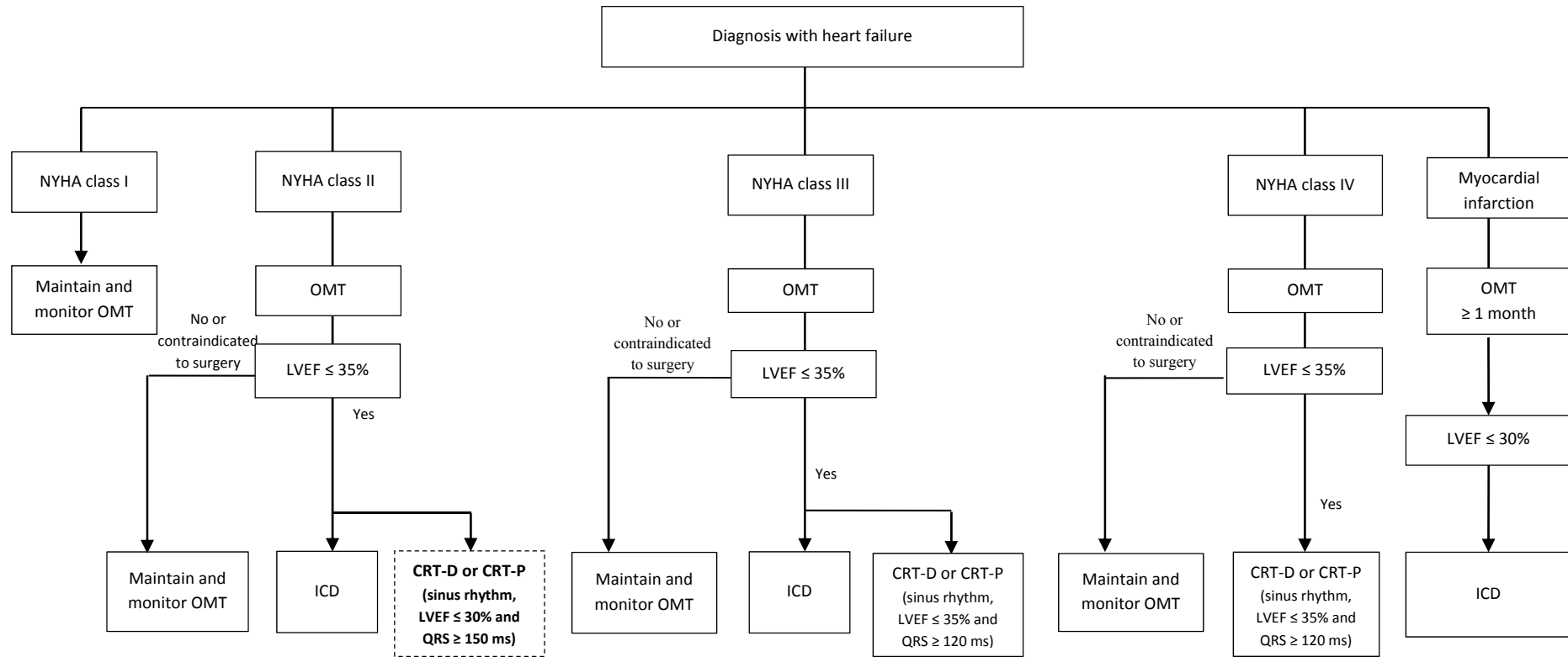
The submission stated that the clinical management algorithms presented are based on current evidence-based clinical practice guidelines for the prevention, detection and management of chronic heart failure in Australia (National Heart Foundation of Australia (NHFA)/CSANZ 2011).

Figure 1 shows the proposed clinical management algorithm for management of patients with NYHA class II heart failure.

The submission indicated that the majority of patients who meet the proposed eligibility criteria would receive CRT-D implantation however, due to comorbidities and other clinical factors, some patients may receive ICD instead of CRT-D. A proportion of patients contraindicated to receive surgery will continue to receive OMT alone.

It was noted that the clinical management algorithm includes CRT-P as an alternative to CRT-D in the proposed population. This inconsistency was not repeated elsewhere, therefore had no impact on the assessment.

Figure 1 Proposed clinical algorithm for management of chronic heart failure



Abbreviations: CRT-D, cardiac resynchronisation therapy device capable of defibrillation; CRT-P, cardiac resynchronisation therapy with pacing; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; OMT, optimised medical therapy

7. Other options for MSAC consideration

Nil.

8. Comparator to the proposed intervention

The comparator for the proposed medical service is ICD with OMT.

The submission indicated that in current Australian practice patients with NYHA class II heart failure and a low LVEF are much more likely to receive an ICD than to receive a CRT-P device or remain on medical therapy alone due to their increased risk of sudden cardiac death (SCD).

The surgical procedures used for ICD implantation are similar to those used for CRT-D implantation. However, CRT-D implantation requires the insertion of a left ventricular (LV) lead.

MBS items 38387 (ICD device) and 38384 (defibrillation leads) were introduced on the Schedule from 1 November 2006 following an MSAC assessment (Reference 32) on ICD therapy for prevention of SCD.

MSAC agreed that ICD is the appropriate comparator in this patient population.

9. Comparative safety

The submission identified 46 publications reporting the results of five randomised controlled trials (RCTs) which compared CRT-D with ICD in patients with NYHA class II heart failure:

- The Resynchronisation–Defibrillation for Ambulatory Heart Failure Trial (RAFT);
- The Multicentre Automatic Defibrillator Implantation Trial with Cardiac Resynchronisation Therapy (MADIT-CRT);
- The Resynchronisation Reverses Remodeling in Systolic Left Ventricular Dysfunction trial (REVERSE);
- The Multicenter InSync ICD Randomized Clinical Evaluation II (MIRACLE ICD II); and
- A trial published by Higgins et al (2003), referred to as the CONTAK-CD trial.

Nine of these publications were systematic reviews that included an assessment of CRT-D versus ICD in patients with NYHA class II heart failure.

Comparative studies and associated reports

The submission presented two key clinical trials, the RAFT and MADIT-CRT, to provide evidence of comparability of CRT-D with ICD in regards to safety.

The REVERSE and MIRACLE ICD II trials were presented to provide supportive evidence for the safety of CRT-D devices. These trials did not directly compare the safety and efficacy of CRT-D with ICD implantation but were designed to compare clinical outcomes occurring in patients who received an active CRT-D implant (CRT-ON), versus patients who received a CRT-D implant programmed to function as an ICD (CRT-OFF).

The CONTAK-CD trial was excluded from evaluation in the submission as the trial was originally designed as a crossover study with two three-month observation periods. The crossover stage was removed partway through the investigation due to regulatory concerns about the insufficient length of follow-up.

RAFT

The RAFT trial was a randomised, double-blind, and multi-centre study. A total of 1,798 patients with either NYHA class II or III heart failure were enrolled to receive OMT with either CRT-D or ICD implantation between 2003 and 2009. The majority of subjects were NYHA class II (80.0%).

Procedure and system related complications (SRCs) were collected throughout the duration of the trial. More of these complications occurred in the CRT-D group (118 subjects) compared to the ICD group (61 subjects) in the first 30 days post-implant. These results were consistent with other studies. Complications included:

- haemothorax or pneumothorax;
- device-pocket haematoma requiring intervention;
- device-pocket infection requiring intervention;
- lead dislodgement requiring intervention;
- device-pocket problems requiring revision; and
- coronary sinus dissection.

MADIT-CRT

MADIT-CRT was a prospective, randomised, controlled, multi-centre study. In total, 1,079 of the 1,820 participants were randomised to receive CRT-D (of whom 1,078 (99%) received a device) and 731 were randomised to receive ICD (of whom 712 (97.4%) received a device). Outcomes in the MADIT-CRT trial included combined NYHA class I and II patients in the ischemic cardiomyopathy subgroup, whereas the non-ischemic cohort included only NYHA class II patients.

Of the patients who underwent an implant procedure, 144 patients experienced SRCs within the first 30 days post-implant; 14 patients experienced SRCs between 31 and 60 days, and six patients experienced SRCs between 61 and 91 days.

Serious adverse events occurring in the first 30 days post-implant included:

- pneumothorax;
- infection;
- device-pocket haematoma requiring evacuation; and
- coronary venous dissection with pericardial effusion.

During long-term follow-up after the first 30 days, serious device-related adverse events occurred with a frequency of 4.5 per 100 device-months in the CRT-D group versus 5.2 per 100 device-months in the ICD group (Moss et al 2009).

The SRC-free rate for participants in the CRT-D group was 84.8% with a lower one-sided 95% confidence bound of 82.9%. This was statistically significantly greater than the pre-specified safety boundary of 70%. Therefore it was concluded that CRT-D systems are safe in patients with NYHA class I or II heart failure, a LVEF of less than 30%, and QRS duration of ≥ 130 ms (MADIT-CRT Clinical Study Report).

REVERSE

The REVERSE trial enrolled a total of 684 patients with NYHA class I or II heart failure, of whom 621 (90.8%) were successfully implanted with a CRT-D or CRT-P device.

The REVERSE trial defined a complication as an adverse event that resulted in invasive intervention or the termination of significant device function regardless of other treatments.

After implantation and during the 12-month follow-up period, 101 of the 621 successfully implanted patients experienced a total of 138 procedure or SRCs. The most common post-implant complications were lead dislodgements (66 cases) and inappropriate device irritation of tissue (e.g. diaphragmatic nerve stimulation, 14 cases). At the time of database closure for the primary analysis, 128 (93%) of post-implant complications were resolved (66% within three weeks of onset), seven were ongoing, two were unresolved with no further actions expected, and one resulted in death.

A total of 66 LV lead-related complications occurred among 59 patients. In 48 cases these required reoperation (8% of successfully implanted patients). The most common types of LV lead-related complications were:

- LV lead dislodgements (41 cases);
- diaphragmatic stimulation (14 cases);and
- subclavian vein thrombosis (3 cases).

In 86% of cases, these complications were resolved without untoward clinical effects (Linde et al 2008).

Complication rates did not differ between treatment groups ($p = 0.64$) and were reported for the trial population as a whole.

MIRACLE ICD II

The MIRACLE ICD II trial examined whether the addition of CRT to an ICD slows disease progression and improves exercise performance in patients with NYHA class II heart failure. A total of 222 participants were enrolled at 51 centres located in the US and Canada. All participants underwent CRT-D implantation.

The MIRACLE ICD II trial collected data on the frequency of complications, defined as a sign, symptom, illness, or other medical event that was resolved invasively or that resulted in the death of or serious injury to a patient, including termination of a significant device function.

Of the 210 participants who underwent CRT-D implantation in the MIRACLE ICD II trial, 46 participants (22%) experienced 56 complications from the time of implant to the time of discharge. Nineteen complications were related to placement of the LV lead including:

- coronary sinus dissection (3 cases);
- cardiac perforation (3 cases); and
- lead dislodgement (5 cases).

From hospital discharge to the end of the six month randomisation period, 109 complications occurred in 66 of 191 participants (35%) with a successful implant, of which 19 were related to the LV lead (Abraham et al 2004).

Overall, MSAC considered that CRT-D was less safe than ICD with statistically significant differences in the rates of complications. However, most of the complications resolved without long-term clinical effects, and that the safety profile of CRT-D was acceptable.

10. Comparative effectiveness

RAFT

In the RAFT trial, subjects were followed for a minimum of 18 months. The primary endpoint was a composite of time to first heart failure hospitalisation or all-cause mortality, with a secondary endpoint of all-cause mortality.

The primary outcome occurred in 364 of 904 subjects (40.3%) in the ICD group and 297 of 894 subjects (33.2%) in the CRT-D group. Regarding the all-cause mortality secondary endpoint, 236 ICD group subjects (26.1%) died versus 186 CRT-D subjects (20.8%).

Eighty percent (80%) of subjects enrolled were classified as NYHA class II. For the NYHA class II subgroup, 253 of 730 ICD group subjects (34.7%) and 193 of 708 CRT-D group subjects (27.3%) met the primary endpoint. In this same subgroup, 154 subjects (21.1%) in the ICD group and 110 subjects (15.5%) in the CRT-D group died.

MADIT-CRT

In the MADIT-CRT trial, the primary endpoint was defined as death from any cause or a non-fatal heart failure event, whichever came first (Moss et al 2009). A higher percentage of patients had a primary event in the ICD group as compared to the CRT-D group. The primary effectiveness endpoint was predominantly driven by a reduction in heart failure events with CRT-D.

REVERSE

The European cohort of the REVERSE trial was followed for 24 months before being unblinded. Within this cohort, 68% of participants received a CRT-D and 32% received a CRT-P. Fewer participants in the CRT-ON group were classified as having a worsened clinical response, compared to the CRT-OFF group. This was attributed to the higher rate of death from any cause or hospitalisation due to or associated with worsening heart failure occurring in the CRT-OFF group (Daubert et al 2009).

MIRACLE ICD II

In the MIRACLE ICD II trial, the composite clinical response system described by Packer et al (2001) was used to assign participants to one of three clinical response categories: improved, worsened or unchanged. Overall, 20% of participants in the CRT-D group were classified as having a worsened overall clinical status, compared with 30.7% of those in the ICD group.

Overall, MSAC considered that the evidence from the RAFT trial for the composite primary effectiveness outcome of death from any cause or hospitalisation for heart failure and the secondary all-cause mortality outcome suggests that the addition of CRT-D to OMT significantly reduces mortality in patients with mild heart failure compared with ICD.

11. Economic evaluation

The economic evaluation presented in the submission was a cost-utility analysis that assessed the incremental cost-effectiveness of CRT-D compared to ICD.

Three published economic evaluations were identified that assessed the cost-effectiveness of CRT-D versus ICD for the treatment of patients with mild (NYHA class I or II) heart failure.

Only one publication was identified that specifically evaluated the cost-effectiveness of CRT-D implantation versus ICD implantation in patients with mild chronic heart failure

(Noyes *et al* 2013). This was based on clinical and health care resource use data collected within the MADIT-CRT trial over a short time horizon of four years. This time horizon does not capture the full period in which the costs and effects of CRT-D treatment would be realised.

However, the evaluation described by Noyes *et al* (2013) accounted for differences in heart failure events and mortality rates, and health care utilisation events including hospitalisations, emergency room visits, physician visits, outpatient surgeries, and diagnostic tests and procedures.

The average four year healthcare expenditures of patients in the CRT-D arm of the MADIT-CRT trial was higher than that of patients in the ICD arm due to differences in device and implant-related costs. It was concluded that CRT-D implantation is cost-effective, compared with ICD implantation, in patients with NYHA class I or II heart failure with a low LVEF and left bundle branch block (LBBB) (Noyes *et al* 2013).

In the full MADIT-CRT population (NYHA class I or II patients) over the short-term it was estimated that the incremental cost-effectiveness ratio (ICER) for CRT-D compared with ICD was around \$58,300 per quality-adjusted life year (QALY). It was noted that this ICER could reduce further if the analysis was conducted over a time period that captured the full costs and benefits associated with CRT-D and ICD implantation.

In the base case analysis (using a life-time horizon), the incremental cost-effectiveness of CRT-D compared to ICD was estimated to be \$27,737.11 per additional QALY gained.

12. Financial/budgetary impacts

The total cost of a successful CRT-D implantation procedure is \$75,060.32 of which \$2,027.73 is incurred by Medicare and private health insurers for medical service fees. The total cost of a successful ICD implantation procedure is \$63,424.33 of which \$1,489.11 is incurred by Medicare and private health insurers for medical service fees.

The base case financial analysis in the submission estimated that 20% of patients receiving MBS item 38387 (ICD) would instead receive CRT-D.

In 2012, the number of patients who received an ICD in Australia reimbursed through the MBS was 742. This is expected to grow to 1,208 patients by 2018, therefore the estimated number of patients expected to be treated with CRT-D would be 242 in 2018.

The financial impact on MBS expenditure of introducing CRT-D was estimated to be \$73,972 in 2014 growing to \$97,582 in 2018. A portion of this would be funded by private health insurers.

The total net financial impact on healthcare expenditure was estimated to be \$2,064,177 in 2014 increasing to \$2,722,999 in 2018. The device costs incurred by private health insurers accounts for approximately 90% of the estimated total net financial impact of reimbursing CRT-D in the proposed MBS indication.

13. Other significant factors

Nil.

14. Key issues for MSAC from ESC

ESC raised concerns that there is a gap in the clinical indication for CRT-D and ICD implantation. Patients with LVEF of 31% to 35% and QRS less than 150 ms will be eligible for ICD implantation but will not be eligible for CRT-D implantation.

ESC considered that the main economic issues were that:

- The utility weights did not greatly alter the ICER based on a 10 year rather than a 20 year extrapolation.
- The base case ICER was approximately \$27,000 per QALY gained however, the ICER was very sensitive to change in the time horizon.
- A 5 year time horizon was extrapolated to 34 years.

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

MSAC considered the application requesting to expand the current MBS items (38371, 38368 and 38654) for the insertion, replacement or removal of a CRT-D and associated leads to include patients with mild chronic heart failure (NYHA class II).

Currently, management of chronic heart failure patients with NYHA class II symptoms with OMT and device therapy is not considered unless the LVEF is $\leq 35\%$. Patients with LVEF $\leq 35\%$ would currently receive an ICD. MSAC noted that the proposed change to the MBS items incorporates a change in clinical management of chronic heart failure for patients with NYHA class II symptoms with an inclusion of CRT in addition to an ICD in certain patients.

MSAC agreed that ICD is the appropriate comparator in this patient population.

MSAC noted that the results for comparative safety and efficacy were largely presented from the RAFT and MADIT-CRT RCTs. The primary effectiveness outcomes of interest specified in the protocol were all-cause mortality, sudden cardiac death, quality of life and rate of hospitalisation. MSAC considered that the RAFT trial was better designed to address the outcome of mortality.

Results for complications during the first 30 days after device implantation in the RAFT trial were 13.3% vs. 6.8% for the CRT-D and ICD groups, respectively. Complications included lead dislodgement (7%), haemothorax, pneumothorax, device pocket infection/ haematoma, and coronary sinus dissection. Results for device related serious adverse events beyond 30 days from the MADIT-CRT trial showed similar rates for the CRT-D and ICD groups (4.5 vs. 5.2 per 100 device-months). Overall, MSAC considered that CRT-D was less safe than ICD with statistically significant differences in the rates of complications. However, most of the complications resolved without long-term clinical effects, and that the safety profile of CRT-D was acceptable.

MSAC considered that the evidence from the RAFT trial for the composite primary effectiveness outcome of death from any cause or hospitalisation for heart failure and the secondary all-cause mortality outcome suggests that the addition of CRT-D to OMT significantly reduces mortality in patients with mild heart failure compared with ICD. Results for the primary outcome in the intention to treat (ITT) population showed that this occurred in 33.2% of the CRT-D group, compared to 40.3% in the ICD group (hazard ratio [HR], 0.75; 95% CI, 0.64 to 0.87; $P < 0.001$). Similar results for the primary outcome were shown for the *a priori* subgroup with NYHA class II heart failure, 27.3% in the CRT-D group, compared to 34.7% in the ICD group (HR, 0.73; 95% CI, 0.61 to 0.88; $P = 0.001$). Results for the

secondary outcome of all-cause mortality showed, for the ITT population, 20.8% in the CRT-D group died, compared with 26.1% in the ICD group (HR, 0.75; 95% CI, 0.62 to 0.91; P=0.003). For the subgroup with NYHA class II heart failure, 15.5% in the CRT-D group died, compared with 21.1% in the ICD group (HR, 0.71; 95% CI, 0.56 to 0.91; P=0.006). In addition, CRT reduces hospitalisations due to heart failure and improves quality of life, and there is evidence that placement of CRT-D results in reverse remodelling of the ventricular wall.

MSAC noted that, based on the evidence presented, the benefit of CRT was confined to patients with a prolonged QRS duration (≥ 120 ms) and that sub-group analysis of the trial populations indicated that the benefit was greater in patients with a QRS ≥ 150 ms compared to those with QRS duration between 120 and less than 150 ms. MSAC considered a QRS < 150 ms was an important exclusion criterion for the proposed MBS item amendments.

MSAC also noted that the trial-based criteria suggest an LVEF cut off of $\leq 30\%$. However, considering the coefficient of variation of echocardiography (10%) for ejection fraction estimation and to match the LVEF cut off for ICD therapy, MSAC concluded that $\leq 35\%$ would be a more suitable cut off and would prevent patients being denied CRT based on readings affected by the margin of error.

The economic evaluation assessed the incremental cost per death avoided for CRT-D over ICD over 60 months, plus a time horizon extension to 20 years including the costs of generator replacements and a time horizon set to lifetime analysis. MSAC noted that this analysis showed that using a CRT-D device over an ICD would cost \$27,737 for each additional QALY gained.

MSAC noted that the financial analysis was based on an estimate that 20% of patients currently receiving ICDs would alternatively receive a CRT-D. Based on MBS data for item 38387, 742 patients received ICDs in 2012; this number is expected to grow to 1208 in 2018. Therefore, according to the proposed changes, by 2018 the number of patients expected to be treated with CRT-D instead of ICD would be 242. The analysis presented in the submission based assessment report estimated that the MBS financial implications of listing CRT-D would be \$73,972 in 2014, growing to \$97,582 in 2018. MSAC noted that the total net financial implications of expanding the MBS restriction to include patients with mild heart failure would be \$2.7 million by 2018.

Lay summary

Chronic heart failure occurs when the heart muscle is weakened and unable to pump as well as it normally does. Patients are generally treated with medicines that can help to improve heart function and reduce hospitalisation and death. Treatment may also include implanting a cardiac device capable of defibrillating the heart and resynchronising heart contractions by sending tiny electrical impulses to help the heart pump blood throughout the body. Defibrillating the heart returns a life-threatening heart rhythm to normal.

MBS items are available for the placement of this device when patients have moderate to severe heart failure. From the evidence presented, implanting a defibrillator capable of resynchronisation has been shown to reduce mortality in patients with mild heart failure. MSAC supported public funding to expand the MBS listing to include patients who have mild heart failure.

16. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to safety, clinical effectiveness and cost-effectiveness, MSAC supports public funding for cardiac resynchronisation therapy with a cardioverter defibrillator by amending the current MBS items 38371, 38368 and 38654 to also include patients who have mild chronic heart failure symptoms (NYHA Class II) despite optimal medical therapy and who meet the following criteria:

- sinus rhythm
- left ventricular ejection fraction of $\leq 35\%$
- QRS duration ≥ 150 ms.

MBS 38371

PERMANENT CARDIAC SYNCHRONISATION DEVICE CAPABLE OF DEFIBRILLATION, insertion, removal or replacement of, for patients who have moderate to severe chronic heart failure (NYHA class III or IV) despite optimised medical therapy and who meet all of the following criteria:

- sinus rhythm
- a left ventricular ejection fraction of less than or equal to 35%
- a QRS duration greater than or equal to 120 ms.

And for patients who have mild chronic heart failure (NYHA class II) despite optimised medical therapy and who meet all of the following criteria:

- sinus rhythm
- a left ventricular ejection fraction of less than or equal to 35%
- a QRS duration greater than or equal to 150 ms. (Anaes.)

Fee: \$287.85 **Benefit:** 75% = \$215.90 85% = \$244.70

MBS 38368

PERMANENT TRANSVENOUS LEFT VENTRICULAR ELECTRODE, insertion, removal or replacement of through the coronary sinus, for the purpose of cardiac resynchronisation therapy, for patients who have moderate to severe chronic heart failure (NYHA class III or IV) despite optimised medical therapy and who meet the following criteria:

- sinus rhythm
- a left ventricular ejection fraction of less than or equal to 35%
- a QRS duration greater than or equal to 120 ms.

And for patients who have mild chronic heart failure (NYHA class II) despite optimised medical therapy and who meet all of the following criteria:

- sinus rhythm
- a left ventricular ejection fraction of less than or equal to 35%
- a QRS duration greater than or equal to 150 ms.

Where the service includes right heart catheterisation and any associated venogram of left ventricular veins. Not being a service associated with a service to which item numbers 38200 and 35200 apply. (Anaes.)

Fee: \$1224.60 **Benefit:** 75% = \$918.45

MBS 38654

PERMANENT LEFT VENTRICULAR ELECTRODE, insertion, removal or replacement of via open thoracotomy, for the purpose of cardiac resynchronisation therapy, for patients who have moderate to severe chronic heart failure (NYHA class III or IV) despite optimised medical therapy and who meet the following criteria:

- Sinus rhythm
- A left ventricular ejection fraction of less than or equal to 35%
- A QRS duration greater than or equal to 120 ms.

And for patients who have mild chronic heart failure (NYHA class II) despite optimised medical therapy and who meet all of the following criteria:

- sinus rhythm
- a left ventricular ejection fraction of less than or equal to 35%
- a QRS duration greater than or equal to 150 ms.

Where the service includes right heart catheterisation and any associated venogram of left ventricular veins. Not being a service associated with a service to which item numbers 38200 and 35200 apply. (Anaes.) (Assist.)

Fee: \$1224.60 **Benefit:** 75% = \$918.45

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

No comment.

18. Context for decision

This advice was made under the MSAC Terms of Reference.

MSAC is to:

Advise the Minister for Health on medical services that involve new or emerging technologies and procedures and, where relevant, amendment to existing MBS items, in relation to:

- the strength of evidence in relation to the comparative safety, effectiveness, cost-effectiveness and total cost of the medical service;
- whether public funding should be supported for the medical service and, if so, the circumstances under which public funding should be supported;
- the proposed Medicare Benefits Schedule (MBS) item descriptor and fee for the service where funding through the MBS is supported;
- the circumstances, where there is uncertainty in relation to the clinical or cost-effectiveness of a service, under which interim public funding of a service should be supported for a specified period, during which defined data collections under agreed clinical protocols would be collected to inform a re-assessment of the service by MSAC at the conclusion of that period;
- other matters related to the public funding of health services referred by the Minister.

Advise the Australian Health Ministers' Advisory Council (AHMAC) on health technology assessments referred under AHMAC arrangements.

MSAC may also establish sub-committees to assist MSAC to effectively undertake its role. MSAC may delegate some of its functions to its Executive sub-committee.

19. Linkages to other documents

MSAC's processes are detailed on the MSAC Website at: www.msac.gov.au.