



## **Medical Services Advisory Committee**

### **Public Summary Document**

#### ***Application No. 1129 – Second Generation Contrast Agents for use in Patients with Suboptimal Echocardiograms***

**Applicant:** Lantheus Medical Imaging Australia Pty Ltd  
**Date of MSAC consideration:** 48th MSAC meeting, 29-30 March 2010

#### **1. Purpose of Application**

An application was received from Lantheus Medical Imaging for funding use of its second generation contrast agent (Definity) in patients with suboptimal echocardiograms through the Medicare Benefits Schedule (MBS).

Second generation contrast agents are proposed for use in patients with suboptimal echocardiograms to opacify the left ventricular chamber and to improve the delineation of the left ventricular endocardial border and assessment of regional wall motion. Despite being submitted as a proprietary application, it is MSAC policy to take a generic approach to assessments, and thus it was agreed that this assessment would be a generic review of all second generation contrast agents. While numerous contrast agents are available, this assessment analysed echocardiography procedures that used either Optison or Definity. These agents are referred to as “second generation” and were the only two second generation contrast agents approved by the Therapeutic Goods Association at the time of the MSAC evaluation.

Therefore, MSAC assessed the use of echocardiography with second generation contrast agents as an alternative or replacement test in patients who have had prior suboptimal echocardiograms without contrast for the following three indications:

1. assessment of ventricular function, ventricular morphology and intra-cardiac masses
2. assessment of risk for ischaemic heart disease using stress echo
3. Doppler evaluation of the left heart

#### **2. Current arrangements for public reimbursement**

There is no MBS item for second generation contrast agents for use in patients with suboptimal echocardiograms.

### **3. Background**

Echocardiography, or cardiac ultrasound, using second generation contrast agents is a noninvasive imaging procedure that provides information on the heart's morphology and function. The technique involves the use of a transducer that transmits high-frequency sound waves towards the heart. The transducer picks up the echoes of the sound waves and transmits them as electrical impulses, which are converted by the echocardiography machine into pictures of the moving heart. The picture is then displayed on a computer screen. No radiation is involved. The second generation contrast agents consist of microbubbles of high-molecular weight gases (e.g. perfluorocarbons) with shells made of either albumin or phospholipids. These contrast agents are injected intravenously in a continuous or bolus dose during the procedure. The microbubbles traverse the pulmonary circulation enabling contrast-enhanced imaging of the left side of the heart. Cardiac echo without contrast can be suboptimal in some patients, due to obesity, lung disease, previous heart surgery or increasing age.

### **4. Clinical need**

Cardiovascular disease is Australia's second highest cause of disease burden, equating to 35% of all deaths in Australia in 2005. It is also one of the leading causes of disability with around 1.4 million Australians (6.9% of the population) estimated to have a disability associated with cardiovascular conditions. In the 2004–05 National Health Survey, about 19% of people surveyed reported one or more long-term diseases of the circulatory system, corresponding to 3.7 million Australians. In relation to direct health care expenditure, cardiovascular disease is the most expensive health condition, costing \$5.9 billion dollars or 11.2% of the total allocated health system expenditure in 2004–05. The cost burden of cardiovascular disease in Australia is expected to increase due to an increasing prevalence of obesity and an ageing population.

Ischaemic heart disease, also known as coronary heart disease or coronary artery disease, is the most common form of heart disease. According to the 2004–05 National Health Survey about 3.2% of Australians have ischaemic heart disease, corresponding to around 637,900 people. It is the largest single cause of death in Australia, accounting for 23,570 deaths (18% of all deaths) in 2005.

Data on the burden of all the diseases or disorders potentially diagnosed by echocardiography are not available; however, many of these diseases and conditions can cause heart failure. People with mild heart failure may have few symptoms, but in more severe cases, patients may be severely limited. These patients have an increased risk of sudden cardiac death. According to the 2004–05 National Health Survey around 263,000 people (1.3% of the population) had heart failure. It contributed to 2,225 deaths in 2005.

MSAC noted that 10-20% of echocardiograms are suboptimal for reasons such as obesity, previous surgery or age. The impact of suboptimal imaging could include incorrect diagnosis or increased flow-on investigations such as nuclear imaging. MSAC noted the claim that optimisation of echocardiography may potentially deliver additional health benefits to patients and also reduce costs by minimizing the number of additional investigations.

MSAC noted that echocardiography is relevant to a wide range of cardiac conditions including heart failure, ischaemic heart disease, structural and congenital abnormalities. It was noted that the current use of echocardiography does not involve intravenous cannulation and that the use of contrast agents would represent a change in practice. The use of contrast enhanced echocardiography would likely suit high-end cardiology providers more so than community cardiologists.

## **5. Comparator**

MSAC noted that two comparators for the three indications were chosen:

- (i) Echocardiogram with contrast (decision to administer contrast made during the echo procedure) compared with echocardiography without contrast.
- (ii) Echocardiography with contrast compared with alternative investigations, such as nuclear imaging (decision to give contrast made after echocardiography)

## **6. Safety**

The MSAC found strong evidence to suggest the use of second generation (intravenous recirculating) contrast agents, when used with echocardiograms, is safe and effective at improving image quality.

Despite a small risk of anaphylaxis, the use of contrast in patients with suboptimal echocardiographic image quality will result in benefits for the consumer by avoiding extra investigations through other imaging modalities, and better informing consumers through more timely diagnosis. If the use of contrast with echocardiograms prevents the need for further investigations that expose the patient to radiation, the use of contrast is comparatively safer.

## **7. Clinical effectiveness**

MSAC agreed the strength of the evidence for clinical effectiveness was satisfactory for Indications 1 and 2 but non-existent for Indication 3 (Doppler evaluation of the left heart).

The use of contrast with echocardiograms produces a considerably clearer image than suboptimal echocardiograms without contrast when assessing ventricular function, ventricular morphology and intracardiac masses. It is also effective for assessing ischaemia in conjunction with stress echocardiography. However, there were no studies identified that evaluated its effectiveness for use with Doppler evaluation of the left heart.

A non-contrast echocardiogram should produce an adequate image in the majority of cases, so contrast should only be used if a non-contrast echocardiogram produces a suboptimal image (approximately 12-15% of cases).

## **8. Cost-effectiveness**

MSAC noted that a cost comparison analysis of the proposed diagnostic approach (echocardiography with contrast) relative to echocardiography alone and the resulting diagnostic pathway was undertaken and subjected to sensitivity analysis.

MSAC found it likely that contrast echocardiograms would obviate the need for more expensive downstream investigations, such as nuclear medicine imaging, resulting in cost savings. There was uncertainty as to what proportion of suboptimal echocardiograms would have further investigations.

MSAC was also concerned about potential for leakage, however noted the procedure requires insertion of an IV cannula and extra time which would serve as a disincentive to performing a contrast echocardiogram on patients for whom it was not needed. It was also noted that there may be an incentive to establish separate “contrast echocardiography” lists which would create an opportunity for two separate MBS billings for echocardiography. The risk of leakage from noncontrast to contrast enhanced echocardiography would be minimised if the MBS fee did not create an incentive.

It was agreed that contrast should not be used when the image quality is satisfactory.

MSAC found the cost saving result is most sensitive to the likelihood of a patient with a suboptimal image receiving a further diagnostic investigation. However, as long as the proportion exceeds five%, the use of contrast is cost-saving.

## **9. Financial/budgetary impacts**

Based on anticipated patient utilisation if listed on the MBS, MSAC estimated savings for the MBS of \$10.35 million for stress echocardiograms and \$19.44 million for rest echocardiograms, with approximately \$2.1 million (stress echo) and \$9.16 million (rest echo and Doppler) in co-payment and out of pocket savings. However, MSAC remained cautious about over-estimating usage and estimated savings.

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

MSAC agreed that second generation (intravenous recirculating) contrast agents, when used with echocardiograms, are safe and are effective at improving image quality. Despite a small risk of anaphylaxis, the use of contrast in patients with suboptimal echocardiographic image quality will result in benefits for the consumer by avoiding extra investigations through other imaging modalities, and better informing consumers through more timely diagnosis. There is satisfactory evidence from prospective cohort studies and studies of diagnostic yield to support this conclusion for the assessment of ventricular function, ventricular morphology (including intracardiac masses) and for the assessment of ischaemia.

MSAC agreed that, due to a reduced use of subsequent health care resources, the economic analyses indicate that, when compared to echocardiography without contrast, rest echocardiography with contrast is cost saving for the assessment of ventricular function, ventricular morphology and intracardiac masses, and stress echocardiography with contrast is cost saving for the assessment of ischaemia.

MSAC was concerned that cost savings may be reduced or potentially eliminated if patients were recalled for another appointment for a repeat echocardiogram to administer the contrast (rather than having the contrast administered as part of the initial study), and/or if the image quality threshold for conducting a contrast-enhanced study (the modelling assumes poor quality images in 12-15%) is lowered over time.

MSAC did not support public funding for Doppler studies of the left heart with contrast on the basis that, although this service may lead to cost savings for society and government compared to alternative investigations, there was no evidence to demonstrate the diagnostic effectiveness of this service.

## 11. MSAC's advice to the Minister

On the strength of the available evidence for safety, effectiveness and cost-effectiveness:

- MSAC supports public funding for the use of a second generation intravenous recirculating contrast agent in a patient undergoing a standard echocardiogram or stress echocardiogram which is suboptimal because:
  - two or more myocardial segments are poorly visualised or
  - assessments of structure and function require higher image quality to improve left ventricular endocardial border delineation.  
(*Indications 1 and 2*)
- MSAC does not support public funding for the use of second generation contrast agents for Doppler evaluation of the left heart. (*Indication 3*)

MSAC requested feedback from the Department after any implementation of this advice in order to verify the modelling assumptions used in this assessment.

## 12. Context for Decision

This advice was made under the MSAC Terms of Reference:

- Advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported.
- Advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness.
- Advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures.
- Undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to the AHMAC.

## 13. Linkages to Other Documents

MSAC's processes are detailed on the MSAC Website at: [www.msac.gov.au](http://www.msac.gov.au).

The MSAC Assessment Report is available at  
<http://www.msac.gov.au/internet/msac/publishing.nsf/Content/completed-assessments>