Australian Government

Medical Services Advisory Committee

MSAC Public Summary Document

Application No. 1098.1 – Review of Interim Funded Service – Breast magnetic resonance imaging (MRI)

Sponsor/Applicant/s: **The Royal Australian and New Zealand College of Radiologists**

Date of MSAC consideration: **MSAC 61st Meeting, 3-4 April 2014**

1. Purpose of application

The application to review the Medicare Benefits Schedule (MBS) interim listing of breast magnetic resonance imaging (MRI) for screening of young women at high risk of breast cancer was submitted in May 2011 by The Royal Australian and New Zealand College of Radiologists.

2. Background

In November 2006, MSAC considered and recommended interim public funding for breast MRI in the diagnosis of breast cancer in asymptomatic women with a high risk of developing breast cancer when used as part of an organised surveillance program.

In February 2009, the Government listed breast MRI on the MBS – item numbers 63464 and 63467 as interim measures.

3. Prerequisites to implementation of any funding advice

The application noted that MRI is currently available in public and private facilities in major centres in each state and territory in Australia.

Breast MRI requires both a breast coil and the use of a gadolinium-containing contrast agent. The Australian Register of Therapeutic Goods lists several coils and gadolinium-containing contrast agents that have been approved by the Therapeutic Goods Administration for use in diagnostic imaging procedures.

4. Proposal for public funding

The application proposed MBS item descriptors are presented below, with the proposed additions to the current wording shown in bold text.

Category 5 – Diagnostic Imaging Services
MBS : 63464 MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where: (a) a dedicated breast coil is used; and (b) the request for scan identifies that the woman is asymptomatic and is less than 50 years of age; and (c)the request for scan identifies either: (i) that the patient is at high risk of developing breast cancer, due to 1 of the following:
(A) 3 or more first or second degree relatives on the same side of the family diagnosed with breast or ovarian cancer; (B) 2 or more first or second degree relatives on the same side of the family diagnosed with breast or ovarian cancer, if any of the following applies to at least 1 of the relatives - has been diagnosed with bilateral breast cancer; - had onset of breast cancer before the age of 40 years; - had onset of ovarian cancer before the age of 50 years; - has been diagnosed with breast and ovarian cancer, at the same time or at different times; - has Ashkenazi Jewish ancestry; - is a male relative who has been diagnosed with breast cancer; (C) 1 first or second degree relative diagnosed with breast cancer at age 45 years or younger, plus another first or second degree relative on the same side of the family with bone or soft tissue sarcoma at age 45 years or younger; or (ii)that genetic testing has identified the presence of a high risk breast cancer gene mutation. **(D) prior history of treatment for invasive breast cancer** **(E) prior history of treatment for Ductal Carcinoma In Situ (DCIS) or Lobular Carcinoma In Situ (LCIS)** **(F) with a history of radiotherapy to the chest area undertaken between the ages of 10-35 years** **Scan of both breasts for:** - detection of cancer (R) Fee: $690.00 Benefit: 75% = $517.50 85% = $618.80 Relevant explanatory note: Bulk bill incentive
MBS 63467 **MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician and where:** **(a) a dedicated breast coil is used; and** **(b) the woman has had an abnormality detected as a result of a service described in item 63464 performed in the previous 12 months** **Scan of both breasts for:** **- detection of cancer (R)** **NOTE 1: Benefits are payable on one occasion only in any 12 month period** **NOTE 2: This item is intended for follow-up imaging of abnormalities diagnosed on a scan described by item 63464** **Bulk bill incentive** **Fee: $690.00 Benefit: 75% = $517.50 85% = $618.80**

5. Summary of Consumer/Consultant Feedback

Public feedback noted that costs for MRI have reduced since 2009. Despite this, the primary concern was that some women may forfeit the necessary testing due to the cost.

6. Proposed intervention's place in clinical management

The application proposed the following changes to the clinical management algorithm:

- no change in the use of breast MRI pathways for the aforementioned cohort of high risk women (presence of genetic mutation or familial history)
- the inclusion of additional high risk patient populations in MBS item 63464. The change in the proposed patient population will see additional patients screened who would not previously have had access to this item

Following the 2006 MSAC assessment, breast MRI was conditionally recommended for use as an additional test (to mammography and ultrasound) in the diagnosis of breast cancer in asymptomatic women with a high risk of developing breast cancer when used as part of organised surveillance.

7. Comparator

The application stated mammography with or without ultrasound as the comparator.

Mammography is the most common form of breast imaging for asymptomatic and symptomatic women.

The MBS also provides a rebate for diagnostic mammography where there is a reason to suspect the presence of a malignancy, for example in women with breast symptoms and women with a personal or family history of breast cancer (MBS items 59300 and 59301). Breast ultrasound may be used to complement mammography (MBS items 55070, 55073 and 55076) with its use varying by centre in Australia.

8. Comparative safety

In 2006 MSAC concluded that, overall, breast MRI was a safe test.

In 2006 the following safety issues were identified:

- Adverse effects of false positive findings (unnecessary investigation)
- Use in patients with contra-indications to exposure to magnetic fields
- Allergy to gadolinium contrast agent
- Claustrophobia which may preclude use in some patients
- Patient discomfort due to the noise of the machine
- Avoidance advised in pregnant women due to limited evidence about the safety of MRI on the developing foetus.

There were no new identified safety risks since MSAC's 2006 consideration.

The application noted the key safety issue with mammography is exposure to ionising radiation.

9. Comparative effectiveness

For the existing breast MRI items, the body of evidence available is largely unchanged (with only one new study) from the MSAC 2006 consideration.

The included studies were:

- MBS interim funded items (asymptomatic high risk women)
    - o two HTA reports
    - o five diagnostic accuracy studies
    - o one patient outcomes study

- Women with a history of breast cancer
    - o two HTA reports
    - o two diagnostic accuracy studies

- Women with a history of DCIS/LCIS
    - o One diagnostic accuracy study

- Women with a history of chest irradiation
    - o three diagnostic accuracy studies

The application noted that none of the studies was assessed as high quality; however, the consistency and precision of estimates of test sensitivity across these studies provide strong evidence that the combination of breast MRI and mammography is a highly sensitive test for the detection of breast cancer (range 0.85 to 0.94, HIQA meta-analysis 0.88 [0.78-0.93]) and offers approximately a 2.3-fold increase in the early detection of breast cancer compared to the use of mammography alone (range 0.36 – 0.40, HIQA meta-analysis 0.38 [0.26-0.51]) in the surveillance of high risk women.

Evidence about the specificity of screening protocols that include breast MRI was less consistent, which may be attributed, at least in part, to the different threshold used to define false positives. The two studies which defined a false positive as a test finding that initiated further testing to exclude malignancy provide the most relevant data and found specificities of 0.77 (0.75-0.79) (Leach 2005) and 0.85 (0.84-0.86) (Kriege et al 2006a), corresponding to a false positive rate of 23% and 15% respectively, compared to a rate for mammography alone of 7% and 5% respectively. Leach (2005) also reported the biopsy rate for false positive imaging which was 5% for MRI plus mammography versus 1.5% for mammography alone.

10. Economic evaluation

A cost-utility analysis, using an Australian adaptation of an economic model developed by the National Institute for Health and Clinical Excellence (NICE) to assess the cost-effectiveness of different surveillance strategies in women at high risk of breast cancer (NICE CG41, 2006), was presented in the application.

The structure of the economic model used in the application was based on the Markov model structure used in the 2006 and 2013 NICE clinical guidelines for familial breast cancer (CG41 and CG164). The model used a one-year cycle length and a lifetime time-horizon. The incremental cost per QALY for the use of MRI plus mammography, compared to mammography alone and based on the current interim-funded fee of $690, was

$35,460/QALY in women with a confirmed mutation for breast cancer, $58,240/QALY in women with a prior history of invasive breast cancer, $82,793/QALY in women with prior history of DCIS/LCIS and the currently reimbursed population with a high familial risk of breast cancer was $91,488/QALY. The ICER was highest in women with a history of chest radiotherapy at $176,536/QALY.

11. Financial/budgetary impacts

The rates of uptake of breast MRI for women with a prior history of invasive breast cancer or prior history of DCIS or LCIS was estimated from the participation rates of the BreastScreen Australia program. The most recent monitoring report for BreastScreen indicated that in 2010-11 the age standardised participation rate was 54.6%. For both populations it was assumed that this uptake rate will begin at 20% in Year 1 of listing, increasing to 54.6% in Year 5.

Data show that, since listing on the MBS on 1 February 2009, 12,046 services and over $7.9 million in benefits have been paid since the current breast MRI items 63464 and 63467 introduction.

Both MBS items, 63464 and 63467, are currently limited to one item in any 12-month period.

The financial cost to the MBS (including the cost of breast MRI, specialist attendance for breast MRI, follow-up biopsy and breast cancer treatment) was estimated to be $8.4 million in 2015 up to $20.3 million in 2019. The total cost to the Government health budgets (including the estimated costs to the MBS, PBS and State and Territory Governments) was estimated to be $9.7 million in 2015 up to $23.3 million in 2019. Cost savings to the MBS come from the replacement of ultrasound with breast MRI. The contribution of follow-up and treatment costs is relatively minor.

Population	**FY 2015**	**FY 2016**	**FY 2017**	**FY 2018**	**FY 2019**
Gene mutation or family history	$3,151,694	$3,558,010	$3,964,326	$4,37,642	$4,776,958
Prior history of invasive breast cancer	$4,665,645	$7,120,865	$9,658,572	$12,277,816	$13,630,036
Prior history of DCIS and LCIS	$551,969	$842,029	$1,141,791	$1,451,502	$1,611,986
Prior history of therapeutic radiation to the chest	$52,469	$106,721	$162,802	$220,759	$255,783
All populations	$8,421,778	$11,627,624	$14,627,624	$18,320,718	$20,274,762

12. Other significant factors

Nil

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

MSAC noted that the application requested a review the current interim funded items 63464 and 63467 for breast MRI screening of high risk women less than 50 years of age. The application also requested to expand item 63464 to include three additional new high risk patient populations, for women less than 50 years of age and have either:

a) a prior history of invasive breast cancer;
b) a prior history of treatment for lobular carcinoma in situ (LCIS) or ductal carcinoma in situ (DCIS); or
c) a history of radiotherapy to the chest area between 10-35 years of age.

MSAC recalled that interim funding for breast MRI screening was supported on the condition that there was a review of the evidence in no less than three years. MSAC noted that the evidence presented to demonstrate the relative effectiveness of adding MRI to standard mammography was limited to studies reporting on diagnostic accuracy; no evidence was presented about the impact of breast MRI screening on patient outcomes.

MSAC noted that there were no new identified safety risks since the 2006 consideration of breast MRI screening.

For the existing MBS item, the evidence base was largely unchanged from the MSAC 2006 consideration; only one new study (Sardanelli et al 2011) was presented. MSAC agreed that the results of this study did not alter the conclusions reached previously by MSAC in 2006. In this population of asymptomatic, high-risk women, who are able to access breast MRI under the current MBS interim item, MSAC noted that the addition of MRI gives a 2.3-fold increase in sensitivity for detection of breast cancer compared to mammography, but a 3-fold increase in investigations for false-positive findings.

For the three additional high risk patient populations:

- the evidence for women with a history of treatment for invasive breast cancer demonstrated that breast MRI screening may offer a two-fold increase in detection of breast cancer and a four-fold increase in the rate of subsequent investigations for false positives;
- for women with a history of treatment for DCIS or LCIS, MSAC agreed that there was insufficient evidence from which to draw any conclusions;
- for women who have had chest irradiation when aged between 10 - 35 years, the results demonstrated that breast MRI screening may offer an approximately 1.4-fold increase in detection of breast cancer and an approximately 1.6-fold rate of biopsy compared to mammography alone.

MSAC considered that the limited evidence presented was weak for these three populations, with a high risk of bias in favour of MRI.

MSAC considered that for all populations, any clinical benefits associated with earlier detection and potential over diagnosis should be weighed against the consequential distress and costs of additional investigations particularly for false positive MRI findings.

The economic evaluation presented was a cost-utility analysis using an Australian adaptation of an economic model developed by the UK National Institute for Health and Clinical Excellence (NICE) to assess the cost-effectiveness of different surveillance strategies in women at high risk of breast cancer. MSAC agreed that the model makes a number of

assumptions that appear biased in favour of MRI. The cost-effectiveness of MRI relied heavily on the assumption that early detection improves 5 year survival by 18.8%, however no outcome data were provided. MSAC considered that the model should have incorporated use of ultrasound. In Australian practice ultrasound may be used as an adjunct to mammography in the diagnostic workup of high risk young women. Inclusion of ultrasound would be expected to reduce the incremental sensitivity of MRI.

Other potential biases in the model included using film-screen mammography as the comparator, which may be inferior to the more commonly used digital mammography, therefore overestimating the incremental benefit of MRI. MSAC considered that, despite potentially favourable biases, the ICERs for the use of MRI + mammography compared with mammography alone for the proposed additional high risk populations were high, uncertain and likely to be underestimated. The differences between the groups driven principally by the baseline risk of breast cancer, the age at which each population begins screening and the population-specific diagnostic accuracy data for MRI + mammography compared with mammography alone.

From sensitivity analyses, MSAC noted that applying a decrement in health-related quality of life for one month in women with false-positive results substantially increases the ICER in populations where there is a relatively low baseline risk of breast cancer, such as those with prior DCIS/LCIS or invasive breast cancer.

MSAC considered that for the high risk patient population covered by the current interim item, the model should include ultrasound as well as adjustment to reflect the exit from surveillance of high risk women who choose to undergo prophylactic mastectomy. Further information should also be provided regarding access to MRI surveillance based on the patient's risk of cancer over the next year or 10 years. MSAC also considered that the assessment report may have underestimated the risk of breast cancer in women with a history of radiotherapy and sought further information on the risk of breast cancer and the role of MRI surveillance in this population.

MSAC considered that the potential utilisation was highly uncertain particularly for patients with a prior history of breast cancer (invasive, DCIS, LCIS), and that expanding the eligible patient population could potential significantly increase utilisation and the potential for leakage.

This uncertainty was also reflected in the financial estimates which are most sensitive to the cost of MRI and associated specialist attendance costs, and to changes in the number of women screened with breast MRI. Changes to in diagnostic accuracy and risk of breast cancer have a moderate impact on the financial estimates because these variables alter number of women who receive biopsy and treatment which account for a small proportion of total cost. MSAC considered that the screening uptake rates for high-risk patients may be underestimated due to these patients being more likely to comply with screening recommendations.

14. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to the safety, clinical effectiveness and cost-effectiveness of breast MRI, MSAC deferred the application for the current interim funded items to seek inclusion of ultrasound in the economic modelling, as well as adjustment to reflect the withdrawal from surveillance of high risk women who choose to undergo prophylactic mastectomy. MSAC discussed that there is currently no MBS item for mammography for asymptomatic patients, and considered the option of the inclusion in the MBS of a mammography item to complement breast MRI for surveillance of high risk patients. Further information should also be provided to support access to MRI surveillance based on the patient's estimated risk of cancer over the next year or 10 years. MSAC suggested lifetime risk of breast cancer >30% and 10-year risk of breast cancer death >8%.

MSAC also deferred the application for the new high risk population of women who have a prior history of radiotherapy to seek additional information regarding breast cancer risk and MRI surveillance. If the interim funded items are reviewed and based on a risk of breast cancer or risk of breast cancer death, this population may fulfil the risk estimates and qualify. Evidence would have to support this.

MSAC did not support public funding for the new high risk populations of women with a prior history of invasive breast cancer and with a prior history of treatment for lobular carcinoma in situ (LCIS) or ductal carcinoma in situ (DCIS) due to uncertain clinical benefit and cost-effectiveness.

MSAC considered that reconsideration should be via ESC and would require external evaluation.

MSAC supported amending the current interim MBS items 63464 and 63467 for breast MRI screening to be gender neutral.

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

No comment.

16. Linkages to other documents

Further information is available on the MSAC Website at: www.msac.gov.au.