



## Medical Services Advisory Committee

### Public Summary Document

#### **Reference No. 44 – KRAS mutation testing for cetuximab (Erbix<sup>®</sup>)**

**Applicants:** Merck Serono Australia Pty Ltd  
Royal College of Pathologists of Australasia

**Date of MSAC consideration:** 51st MSAC meeting, 2 December 2010

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

In October 2010 an application requesting MBS listing of KRAS gene mutation testing of metastatic colorectal cancer (mCRC) tumours was received from Merck Serono Australia Pty Ltd, in conjunction with the Royal College of Pathologists of Australasia.

The July 2010 Pharmaceutical Benefits Advisory Committee (PBAC) meeting recommended an extension of the current Authority Required listing of cetuximab (Erbix<sup>®</sup>) on the Pharmaceutical Benefits Scheme (PBS) to include initial and continuing treatment as monotherapy or in combination with an irinotecan based chemotherapy following failure of chemotherapy in KRAS wild type patients with metastatic colorectal cancer (mCRC). Accordingly, the PBAC recommendation requires that the KRAS gene mutation status of the patient's tumour be ascertained in order to determine eligibility for any PBS-subsidised cetuximab treatment in mCRC. As determination of KRAS gene status is not currently covered under any existing MBS item, the purpose of the current application is to seek public funding of KRAS gene mutation testing of tumour specimens from patients with mCRC.

The indication requested for the proposed service was: "Determination of tumour KRAS mutation status by molecular techniques prior to the initiation of cetuximab therapy in patients with metastatic colorectal cancer".

The therapeutic claim made by Merck Serono is that the absence of a KRAS gene mutation in mCRC is predictive of a more favourable clinical response and better long term outcomes, including a significantly longer survival time, with cetuximab treatment.

There has been no previous MSAC consideration of KRAS gene mutation testing. The intention of this testing is to identify patients with KRAS gene mutations because they would be unlikely to respond to cetuximab therapy. As such, KRAS gene mutation testing is considered as a co-dependent technology with cetuximab.

## 2. Current arrangements for public reimbursement

The proposed service is not covered under any existing MBS item. Currently, patients would access this test either via participation in clinical trials, by paying the cost of testing themselves or by participating in the Sponsor's KRAS gene testing Access Program.

Category PATHOLOGY P7 – GENETICS
Determination of tumour KRAS mutation status by molecular techniques prior to the initiation of cetuximab therapy in patients with metastatic colorectal cancer.
Proposed MBS Fee: \$250

MSAC found that the proposed fee was based on expert opinion (ie market testing) and not on a breakdown of resource inputs. MSAC also noted that, if listed on the MBS, the proposed fee would be higher than any current genetic test in the Pathology Services Table.

MSAC also found uncertainty in relation to whether or not the proposed fee included the costs of retrieving the sample (which was taken at the point of initial diagnosis) to assess mutation status when the cancer progresses, or any need to obtain a new sample from some patients.

MSAC accepted that the comparator is “no testing”. KRAS gene mutation testing would not be replacing any other current routine diagnostic service as until now there has been no reason to test mCRC tumours for KRAS gene mutations.

## 3. Background

Data from the Australian Institute of Health and Welfare (AIHW) indicate that each year over 13,000 individuals are diagnosed with colorectal cancer in Australia (AIHW, 2007). Of those, 50-60% of patients will go on to develop metastatic disease requiring surgery, chemotherapy or a combination of the two for treatment (Engstrom et al., 2009). First-line systemic treatment for metastatic colorectal cancer includes combinations such as fluorouracil and folinic acid (leucovorin) plus either irinotecan (FOLFIRI) or oxaliplatin (FOLFOX), or bevacuzimab and fluorouracil. Once patients develop progressive disease on first line treatment, the prognosis is poor.

The applicant claims that cetuximab therapy offers an effective second-line treatment to improve the survival specifically of a subgroup of patients identified through KRAS gene testing. MSAC noted that the clinical need and public health significance of KRAS gene testing in mCRC has already been established through the PBAC process and is confirmed by the PBAC decision to recommend cetuximab therapy for public funding.

Determination of tumour KRAS gene mutation status prior to second-line chemotherapy with cetuximab in patients with mCRC.

Several molecular tests are used to determine tumour Kirsten ras (KRAS) mutation status in patients with mCRC. KRAS gene testing can be performed on either fresh frozen (FF) or formalin fixed paraffin embedded (FFPE) tissue. Testing can therefore be performed retrospectively on archived blocked tissue samples of the primary tumour that may have been surgically resected years earlier. Since tumour specimens may need to be tested for KRAS gene mutation status in the future, the Royal College of Pathologists of Australasia (RCPA) suggests it is desirable for the reporting pathologist to designate a block of tissue from all CRC resections that contains a high proportion, preferably over 70%, of cancer tissue.

The purpose of testing is to identify patients with KRAS wild type mCRC who would be eligible to receive PBS-subsidised treatment with cetuximab and to exclude PBS subsidy from this therapy those patients with tumours identified as KRAS mutant type. Patients with tumours of KRAS mutant type do not respond to cetuximab therapy.

Although KRAS gene testing is considered a diagnostic investigation (as opposed to a procedure or other service), it is not intended for use in screening patients for or in making a diagnosis of CRC.

Currently in Australia, KRAS gene mutation testing is performed by several NATA-accredited pathology laboratories.

Resources required for the intervention include experienced laboratory technicians (salary); retrieval of tumour specimens (usually formalin fixed paraffin embedded tissue from the primary tumour); possible costs of repeat biopsy if a primary tumour sample is not available; KRAS gene mutation test – reagents, instrumentation – varies depending on test methodology; as well as administrative costs.

If the tumour sample to be tested did not originate from the testing laboratory, then tumour tissue blocks or sections would be located and obtained from the laboratories where they were prepared following tumour resection/biopsy, along with the associated pathology report. The retrieval process may take between several days and two or three weeks.

Ordinarily, the test would be ordered by the oncologist whilst the patient with mCRC is still being treated in a first-line setting. Knowing the patient's KRAS gene status prior to commencing second-line treatment of mCRC may allow for optimal treatment planning and provide sufficient time to retrieve the archived pathology specimen (often from other laboratories) so as to perform the KRAS test.

The choice of method to be employed in KRAS gene mutation testing should be determined by the laboratory director and will depend on the experience, expertise and equipment available in each laboratory and the type of specimen to be examined.

Regardless of the method to be used, a pathologist must select the tissue sample or area to be provided for DNA extraction to ensure that adequate and representative tumour tissue and appropriate normal tissues are assessed.

Any KRAS gene mutation testing funded through the MBS should be performed in a NATA-accredited laboratory that has been demonstrated, in a suitable External Quality Assurance Program (QAP), to be proficient in the technique employed. MSAC noted that the RCPA will have a KRAS gene mutation testing QAP in place by the end of 2010 and that the Department of Health and Ageing will ensure appropriate mechanisms are in place before any MBS listing of the test.

KRAS gene mutation testing would not be replacing any other current routine diagnostic service as until now there has been no reason to test mCRC tumours for KRAS gene mutations, but it would address an unmet need in that there is no existing Medicare benefit payable for KRAS gene testing; patients with mCRC can only access cetuximab on the PBS if their tumour expresses wild type KRAS; and KRAS gene testing is currently provided by the sponsors under their KRAS gene testing access program (expires 1 December 2010), in the setting of clinical trials, or patients fund the test themselves so they can determine their eligibility to access the drug.

The application does not present a description of the proposed clinical management of a typical patient up to the point of being offered KRAS gene testing (and subsequent therapy with/without cetuximab), nor a comparison with the currently existing clinical pathway(s) where KRAS gene testing is not offered.

The co-applicants acknowledged that their proposed approach may lead to testing of some (20%) patients who will not progress to second-line therapy because they are either cured, become too ill to tolerate or are ineligible for further treatment, or who die before second-line treatment can be initiated. The oncology community has advised that it is preferable to perform these extra tests rather than unnecessarily delay treatment for patients with progressive disease.

#### **4. Clinical need**

The estimated prevalence of persons with colorectal cancer in the Australian population is 42,000 cases. However metastatic CRC has a high mortality, so only 20% of these prevalent cases currently have metastatic disease. Cetuximab therapy is provided as a second-line treatment to improve the survival of a subgroup of these patients that can only be identified through KRAS testing. Potentially 5387 patients would be tested per year, with 1077 potentially tested but not needing treatment.

In appraising the place of KRAS gene testing to support the PBAC-recommended use of cetuximab, MSAC considered the point in the clinical pathway of managing colorectal cancer at which a patient's tissue sample should be tested. MSAC considered several additional sensitivity analyses which confirmed that cost-effectiveness was not particularly sensitive to testing at the point of initial diagnosis, at confirmation of metastatic disease or after failure of first-line therapy for metastatic disease. From a clinical perspective, testing should not be delayed until after failure of first-line therapy for metastatic disease because, at a time when the test result is urgently needed (so that second-line treatment could commence without undue delay), this would either require the cost and patient risk of obtaining a new tissue sample, or the cost and delay of retrieving a stored sample. Although logistically simpler to test every patient with colorectal cancer (stages I-IV) at the point of initial diagnosis, the saving of costs associated with retrieving stored samples from patients with relapsed metastatic disease would be outweighed by the extra number of KRAS tests performed. This is true even if this were targeted to patients identified at presentation as being most likely to develop metastatic disease, an option which would have introduced some uncertainty because of difficulties in reliably predicting relapse at initial diagnosis. So from a clinical perspective, and taking into consideration overall costs, MSAC recommended that any MBS item descriptor should specify that the test be eligible for reimbursement when the patient is diagnosed with metastatic disease, when it is clinically anticipated that the patient may require second-line therapy.

The estimated population of patients with colorectal cancer who would go on to have metastatic cancer requiring testing for later eligibility for cetuximab is estimated at 7000 per year. One test result is required per cancer.

#### **5. Comparator**

There is no current equivalent comparator test listed on the MBS, therefore the comparator is "no testing".

The test is to enable patients access to a cetuximab which is only beneficial and cost-effective in patients with responsive tumours.

MSAC noted that if the test is not listed on the MBS, this could potentially mean that 60-65% of patients with mCRC who have wild type KRAS would remain ineligible to receive cetuximab resulting in reduced disease-free survival; or if patients chose to pay for the test themselves, this could result in inequity of care/access to treatment issues.

## **6. Scientific basis of comparison**

The evidence base used in the application is the presentation of overall agreement data from 10 studies comparing different molecular test options to assess the KRAS gene in tumour material.

PBAC reviewed evidence of cetuximab clinical performance based on the CO17 trial (Karapetis et al, 2008) and other trials – not re-evaluated by MSAC.

MSAC noted areas of clinical uncertainty around which molecular test for KRAS should be performed; whether the test should be done on the primary or metastatic tumour tissue; and the potential interplay of other modifiers, e.g., BRAF gene mutations, in the future.

MSAC noted that PBAC had assessed overall clinical effectiveness, but unresolved issues included a lack of direct evidence to specify thresholds of test performance with regard to sensitivity and specificity to ensure optimal use of cetuximab in this setting; a lack of direct evidence to specify thresholds of mutant load at which KRAS mutant status is ascertained; a paucity of evidence on the frequency of tissue-specific KRAS gene mutations in metastases, a paucity of evidence on the significance of KRAS gene mutations (eg G13d); and a paucity of evidence on the significance of mutations in other genes (eg tumours with wild-type KRAS gene and mutant BRAF gene (V600E) are resistant to cetuximab).

MSAC concluded that for these reasons, a QAP with NATA accreditation would be essential prior to any MBS listing.

## **7. Safety**

MSAC agreed that the KRAS test is safe for patients as it uses a sample already collected for histological assessment from patients diagnosed with metastatic CRC. The only time when an additional biopsy might be required is if an original tumour specimen is unable to be retrieved from archive, or was not archived. MSAC noted that the need to obtain new samples due to losses or inadequacies of stored samples should be small. However, pathology laboratories could improve the process of retrieval of such samples by ensuring that each sample is of adequate quality and clearly identified at the time that it is stored.

Test safety is unlikely to be a cause for concern if there are processes in place to efficiently store and retrieve archived tumour samples and if the tests used to determine KRAS gene mutation status are highly sensitive.

## **8. Clinical effectiveness**

At its July 2010 meeting, PBAC considered that cetuximab was effective primarily on the basis of evidence provided in the CO17 trial for the second-line setting of metastatic colorectal cancer (mCRC), which demonstrated an incremental overall survival benefit of 4.7 months (0.39 incremental life-years gained) with the addition of cetuximab to best supportive care compared to best supportive care alone in the subgroup of patients with wildtype KRAS tumours. PBAC acknowledged that the population included in the CO17 trial was not entirely representative of all groups of patients that would be treated with cetuximab under its recommended PBS listing, but considered that the entire body of published evidence supported the use of cetuximab as monotherapy or in combination with irinotecan based chemotherapy in such a setting.

MSAC found that the consequential impact of false negative test results for KRAS mutant status (that is a false conclusion of 'wild type' KRAS status) would be to subject patients who have tumours that are KRAS mutant to treatment with cetuximab. As such, these patients are likely to experience a relatively unfavourable outcome as they may experience adverse effects without any benefit, and may forfeit an opportunity for other beneficial treatment. However, the evidence available suggests that this would occur with less than 2% of test results.

MSAC also found that the consequential impact of false positive test results for KRAS mutant status would be to deny access to the potential benefits of cetuximab. The evidence available suggests that this would occur with less than 18% of test results.

MSAC noted that both these consequential impacts were implicit in the matters already considered by PBAC.

MSAC noted that a range of test options could be used, with some variability across their analytical performance. No test option has been established as the reference standard and no test option was clearly defined as being used across all the randomised trial evidence relied upon by PBAC to conclude that KRAS wild type status predicts a greater effectiveness of cetuximab in particular clinical circumstances. This means that MSAC has to rely on data on concordance or agreement between test options rather than on objective evidence of analytical validity against a reference standard, which hinders complete assessment of the negative consequences of incorrect test results to the health outcomes for patients and to the overall cost-effectiveness of the co-dependent technologies. However as the test performance data indicate a high level of agreement and that overall cost-effectiveness is not sensitive to test performance, MSAC accepted that this type of data provided a sufficient evidentiary basis in this context. However it means that no particular test options or test performance thresholds can be specified in this instance.

In order to address the concerns of possible false negatives, the test should be performed in a NATA accredited laboratory, and be ordered by an oncologist. It should also be supported by a suitable quality standard and a quality assurance program specific to KRAS gene testing developed by RCPA.

## **9. Economic evaluation**

Details of the model structure were not presented in the MSAC application. The economic evaluation of KRAS gene mutation testing is largely based on the cost-effectiveness of cetuximab as presented in the minor submission considered by PBAC in July 2010. The economic evaluation costed KRAS gene mutation testing for all patients tested, regardless of whether they were wild type or not. The proposed MBS fee per test of \$250 was the value included in the economic model submitted to PBAC to assess the cost-effectiveness of cetuximab.

PBAC recommended listing of cetuximab on the PBS as an Authority Required item for the treatment of metastatic colorectal cancer in patients who meet certain criteria on the basis of high but acceptable cost-effectiveness compared with best supportive care. This recommendation was primarily based on the evidence in the CO17 trial with a base case of 0.25 extra QALYs gained, as presented in two previous submissions. PBAC accepted the QALY estimate as reasonable for the base case and considered the impact on overall cost-effectiveness of varying this estimate in sensitivity analyses.

The model did not adequately capture all of the factors that determine whether testing for KRAS gene status is cost-effective. Although a unit cost of the test was included in the model, data on test performance (negative/positive predictive values and the impact of false negative and false positive tests) were not incorporated into the model. Similarly, the impact of unevaluable samples and the need for any additional biopsies were not addressed in the model. While sensitivity analyses indicate that the incremental cost effectiveness ratio is not particularly sensitive to varying the test unit cost or need for additional biopsies, the cost-effectiveness is less favourable at higher test costs and increased biopsies.

The suggested MBS fee was given as \$250 which is comparable to an existing MBS item for a service of a similar complexity with similar reagent costs and scientific staff labour costs. A slightly higher fee was suggested for the KRAS assay because KRAS gene testing may involve retrieval of tissue blocks or unstained slides from external laboratories and required a pathologist to view the slides and select the area for DNA extraction. However, MSAC questioned whether the proposed fee was adequately justified and noted that the MBS fee would be set after consultation between the Department and the pathology profession prior to any MBS listing.

The economic assessment did not address the cost of the test to various payers, including the Australian Government, State and Territory Governments, and for patient co-payments.

The economic assessment did not address the impact on the Medicare Safety Net, although it is not expected to have a significant impact.

MSAC also noted that the overall cost-effectiveness assessment had not fully taken into consideration the logistics and costs for retrieval of samples and the possibility of needing new samples in some circumstances. MSAC agreed that the weight of evidence supported the use of tissue samples taken at diagnosis rather than taking a new sample at the time of progression to metastatic disease because of evidence that the KRAS gene mutation manifests early in the disease and is relatively stable during disease progression.

MSAC found uncertainties with costing of the test, including proportion of patients with available samples, cost of block retrieval, cost of sample assessment for tumour load, and cost of assay and reporting.

## **10. Financial/budgetary impacts**

MSAC noted that restricting public funding of testing for KRAS gene mutation status to patients with metastatic colorectal cancer would limit the use of the test to the initial prevalent pool of approximately 8,500 patients and the annual incident population of metastatic colorectal cancer (estimated at approximately 7,000 patients). Only one test result is needed per cancer because KRAS gene mutation status is relatively stable in a patient over time, and there is no other role for the test (e.g., for prognosis or to monitor the impact of cetuximab).

A total of 7000 patients in Australia are estimated to require a KRAS gene mutation test in year 1. At a fee of \$250 per test, the financial impact of KRAS gene mutation testing is expected to be \$1.75 million per annum, although MSAC suspected that retrieval costs may not have been adequately captured in this estimate.

It is difficult to determine the initial cost because the larger number of prevalent patients is balanced to some extent by a delay in the uptake of testing and the program of free testing recently funded by the sponsor of cetuximab.

Given that stored samples should be retrieved for those patients who do not present initially with metastatic disease, the overall cost of testing would be greater than the cost to the MBS because the costs of retrieval do not currently accrue to the MBS.

MSAC noted that the proposed fee for the tests to determine KRAS gene status did not have a strong justification. Given that overall cost-effectiveness of treatment with cetuximab is not particularly sensitive to the fee for KRAS gene testing, MSAC advised the Department to develop a fee for MBS purposes which would reasonably reflect actual costs, noting that these may be affected by economies of scale.

## **11. Other significant factors**

MSAC suggested that future consideration of co-dependent tests and drugs should ideally be coordinated with input from PBAC, Pathology Services Table Committee (PSTC), National Pathology Accreditation Advisory Council (NPAAC) and the Royal College of Pathologists of Australasia (RCPA).

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

MSAC noted that cetuximab had been recommended by the Pharmaceutical Benefits Advisory Committee (PBAC) for PBS-subsidised use in patients with KRAS wild type metastatic colorectal cancer, whose disease has progressed despite first-line therapy. This recommendation was based on an assessment of clinical and cost-effectiveness which had incorporated information on the associated use of testing for KRAS gene status. Sensitivity analyses conducted as part of this assessment had indicated that overall cost-effectiveness was not particularly sensitive to the performance characteristics of the test options or to their unit cost.

In appraising the place of KRAS gene testing to support this recommended use of cetuximab, MSAC considered the point in the clinical pathway of managing colorectal cancer at which a patient's tissue sample should be tested. MSAC considered several additional sensitivity analyses which confirmed that cost-effectiveness was not particularly sensitive to testing at the point of initial diagnosis, at confirmation of metastatic disease or after failure of first-line therapy for metastatic disease. From a clinical perspective, testing should not be delayed until after failure of first-line therapy for metastatic disease because, at a time when the test result is urgently needed (so that second-line treatment could commence without undue delay), this would either require the cost and patient risk of obtaining a new tissue sample, or the cost and delay of retrieving a stored sample. Although logistically simpler to test every patient with colorectal cancer (stages I-IV) at the point of initial diagnosis, the saving of costs associated with retrieving stored samples from patients with relapsed metastatic disease would be outweighed by the extra number of KRAS tests performed. This is true even if this were targeted to patients identified at presentation as being most likely to develop metastatic disease, an option which would have introduced some uncertainty because of difficulties in reliably predicting relapse at initial diagnosis. So from a clinical perspective, and taking into consideration overall costs, MSAC recommended that any MBS item descriptor should specify that the test be eligible for reimbursement when the patient is diagnosed with metastatic disease, when it is clinically anticipated that the patient may require second-line therapy.

MSAC noted that a range of test options could be used, with some variability across their analytical performance. No test option has been established as the reference standard and no test option was clearly defined as being used across all the randomised trial evidence relied upon by PBAC to conclude that KRAS wild type status predicts a greater effectiveness of cetuximab in particular clinical circumstances. This means that MSAC has to rely on data on concordance or agreement between test options rather than on objective evidence of analytical validity against a reference standard, which hinders complete assessment of the negative consequences of incorrect test results to the health outcomes for patients and to the overall cost-effectiveness of the co-dependent technologies. However as the test performance

data indicate a high level of agreement and overall cost-effectiveness is not sensitive to test performance, MSAC accepted that this type of data provided a sufficient evidentiary basis in this context. However it means that no particular test options or test performance thresholds can be specified in this instance.

MSAC further noted the importance of appropriate collection and handling of test samples as a prerequisite for delivering an adequate sample to ensure optimal test performance. MSAC recommended that quality standard and a quality assurance (QA) program be developed by the Royal College of Pathologists of Australasia (RCPA) to ensure the tests perform to the standard as established for the evidence base relied on by PBAC in recommending the drug as a pharmaceutical benefit. The RCPA should define standards which appropriately address issues such as sample collection, storage and retrieval. MSAC further agreed that any description of the test options should be adaptable to changing indications, noting that there is currently no clear evidentiary basis to use KRAS gene testing for any other purpose, including diagnosis or prognosis of disease or use in association with any other drug. Testing should be performed in a NATA accredited laboratory, and should be ordered by an oncologist.

MSAC also noted that the overall cost-effectiveness assessment had inadequately taken into consideration the logistics and costs for retrieval of samples and the possibility of needing new samples in some circumstances. MSAC agreed that the weight of evidence supported the use of tissue samples taken at diagnosis rather than taking a new sample at the time of progression to metastatic disease because of evidence that the KRAS gene mutation manifests early in the disease and is relatively stable during disease progression. MSAC noted that the need to obtain new samples due to losses or inadequacies of stored samples should be small. However, pathology laboratories could improve the process of retrieval of such samples by ensuring that each sample is of adequate quality and clearly identified at the time that it is stored.

MSAC noted that limiting public funding of testing for KRAS gene mutation status to patients with metastatic colorectal patient would limit the use of the test to the initial prevalent pool of approximately 8,500 patients and the annual incident population of metastatic colorectal cancer (estimated at approximately 7,000 patients). Only one test result is needed per cancer because KRAS gene mutation status is relatively stable in a patient over time, and there is no other role for the test, eg for prognosis or to monitor the impact of cetuximab. At a proposed fee of \$250, the annual cost to the MBS would therefore be approximately \$1.75 million. It is difficult to determine the initial cost because the larger number of prevalent patients is balanced to some extent by a delay in the uptake of testing and the program of free testing recently funded by the sponsor of cetuximab.

Given that stored samples should be retrieved for those patients who do not present initially with metastatic disease, the overall cost of testing would be greater than the cost to the MBS because the costs of retrieval do not currently accrue to the MBS.

MSAC noted that the proposed fee for the tests to determine KRAS gene status did not have a strong justification. Given that overall cost-effectiveness of treatment with cetuximab is not particularly sensitive to the fee for KRAS gene testing, MSAC advised the Department to develop a fee for MBS purposes which would reasonably reflect actual costs, noting that these may be affected by economies of scale.

MSAC suggested that future consideration of co-dependent tests and drugs should ideally be coordinated with input from PBAC, Pathology Services Table Committee (PSTC), National Pathology Accreditation Advisory Council (NPAAC) and the Royal College of Pathologists of Australasia (RCPA).

### **13. MSAC's advice to the Minister**

MSAC supports public funding of testing to determine tumour KRAS mutation status to contribute to the determination of eligibility for PBS-subsidised cetuximab for a patient with metastatic colorectal cancer.

Testing should be performed in a NATA accredited laboratory, and be ordered by an oncologist. It should also be supported by a suitable quality standards and a quality assurance program specific to KRAS testing developed by RCPA.

Draft item descriptor:

*A test of the tumour from a patient with metastatic colorectal cancer to determine if the requirements relating to KRAS gene mutation status for access to cetuximab under the Pharmaceutical Benefits Scheme (PBS) are fulfilled.*

### **14. Context for Decision**

This advice was made under the MSAC Terms of Reference.

“MSAC is to:

Advise the Minister for Health and Ageing on medical services including those 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 such sub-committees.”

### **15. Linkages to Other Documents**

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

More information is available on the home page for Reference 44:

<http://www.msac.gov.au/internet/msac/publishing.nsf/Content/ref44-1>