



Medical Services Advisory Committee Public Summary Document

Reference No. 35d(ii) – Positron Emission Tomography for Sarcoma

Applicant: Diagnostic Services Branch,
Department of Health and Ageing

Date of MSAC consideration: 48th MSAC meeting, 29-30 March 2010

1. Purpose of Application

This referral is a second phase assessment of positron emission tomography (PET) by the Department of Health and Ageing who requested the Medical Services Advisory Committee (MSAC) to review PET for public funding in relation to head and neck cancer, oesophageal gastric cancer, lymphoma, glioma, sarcoma, cervical cancer and ischaemic heart disease. The conclusion of the 2000 Review was that at that time there was 'insufficient evidence from which to draw definitive conclusions about the clinical effectiveness and cost effectiveness of PET' to warrant unrestricted Medicare Benefits Scheme (MBS) funding. As a consequence of the Review, interim funding was extended to seven PET facilities on the condition that data be collected for further evaluation of PET in Australia.

An application from the Diagnostics and Technology Branch (now Diagnostics Services Branch), Department of Health and Ageing was made to MSAC to review the value of PET using F-18 fluorodeoxyglucose (FDG) for:

1. initial *grading* and *guiding biopsy* of suspected sarcoma
2. initial *staging* of biopsy proven bone or soft tissue sarcoma considered potentially curable on conventional staging (*adult-type tumours*)
3. initial *staging* of biopsy proven bone or soft tissue sarcoma considered potentially curable on conventional staging (*paediatric-type tumours*)
4. evaluation of *suspected residual or recurrent sarcoma* after definitive treatment
5. initial *staging* of patients with newly diagnosed *gastrointestinal stromal tumours* (GIST) or with recurrent GIST after locoregional therapy
6. investigation of *suspected progression or treatment resistance* in patients with *GIST*.

2. Current arrangements for public reimbursement

The MBS interim funding arrangement (Item number 61534), due to cease on 1 July 2010, provides reimbursement for whole body FDG PET study to guide biopsy of a suspected bone or soft tissue sarcoma, where structural imaging suggests lesional heterogeneity, with catheterisation of the bladder.

3. Background

PET is a nuclear imaging technique using a short lived radiopharmaceutical (in this instance 2-¹⁸F-fluoro-2-deoxy-D glucose, FDG). The technique provides functional and metabolic information and current scanners incorporated CT in the same instrument. PET/CT may be complemented by anatomical imaging with magnetic resonance imaging (MRI).

Sarcomas are a highly heterogeneous group of tumours of mesenchymal cell origin that account for around 1% of adult and 15% of paediatric malignancies. They can be broadly grouped into two categories: soft tissue sarcomas and primary bone sarcomas.

Soft tissue sarcoma describes tumours occurring in various tissues, including muscle, fat, fibrous and other supporting bodily tissue, and in bone. Gastrointestinal stromal tumours (GIST) are a subset of soft tissue sarcomas that can develop along the gastrointestinal tract and occasionally in the peritoneum. Patients with suspected bone or soft tissue sarcoma conventionally undergo magnetic resonance imaging (MRI) and CT or ultrasound, to determine the local extent of the tumour, its relationship to major tissue compartments and the presence of distant metastases, followed by CT-guided biopsy or surgical pathology to determine tumour type and grade. Metabolic imaging with FDG PET can also potentially guide biopsy to the most metabolically active areas, and thereby may allow more representative tumour grading, as well as providing initial staging information (distant metastases), and detecting tumour recurrence after treatment.

4. Clinical need

In Australia, there were 900 cases reported in 2005 (including soft tissue and bone sarcomas). Gastrointestinal stromal tumours (GISTs) are a rarer subset with approximately 198-320 cases per year in Australia.

MSAC acknowledged that sarcomas are highly malignant tumours, and that improvements in staging, response to treatment, and assessment of disease relapse are needed given the generally poor outcome of these diseases.

5. Comparator

The appropriate comparators for the role of PET scanning are CT and MRI scanning as prior tests. PET scanning is now combined with CT in the one instrument giving both metabolic and anatomic data. MSAC noted that many patients will have had prior diagnostic CT scans in a dedicated CT scanner, and that MRI, depending on circumstances, may add critical additional local anatomic data which is particularly important when surgery is considered.

6. Safety

PET and PET/CT are considered safe procedures. Patients undergoing PET/CT will be exposed to low doses of ionizing radiation, but potential benefits outweigh radiation risks given the known aggressiveness of these malignancies.

7. Clinical effectiveness

MSAC noted there was no direct evidence comparing health outcomes of patients with sarcoma, including GIST, managed with and without PET scanning.

MSAC acknowledged that paediatric-type sarcomas are treated more aggressively with curative intent, whereas patients with adult-type tumours who have metastatic disease are not candidates for treatment with curative intent.

MSAC found that PET for initial grading and guiding of biopsy is at least equivalent to CT or MRI for selection of an appropriate site for biopsy, but no advantage in grading could be confirmed for PET. MSAC found insufficient evidence of incremental benefit of PET versus MRI or CT.

MSAC found that the use of PET for initial staging of biopsy-proven bone or soft tissue sarcoma considered potentially curable on conventional staging more accurately detects metastases (except

for pulmonary metastases) in adult-type tumours. MSAC agreed the evidence base is not strong, but that PET is likely to change patient treatment (from curative to palliative in a proportion of patients with PET-identified additional metastases). This would likely avoid inappropriate attempts at curative therapy (predominantly surgery) and thus improve quality of life in a proportion of those patients with more advanced disease. MSAC agreed there was therefore potential for cost-savings in this setting, but that the magnitude could not be quantified.

MSAC found that PET for initial staging of biopsy-proven paediatric-type sarcoma more accurately detects bone and lymph node metastases (but not pulmonary metastases), with increased costs for a benefit of uncertain magnitude, and in some patients who had otherwise unsuspected metastases there may be changes in treatment with the more appropriate use of escalated versus standard chemotherapy, which may improve disease-free or overall survival. Although the evidence is not strong, the more appropriate use of curative treatment is likely to have a greater impact on health outcomes in this overall younger population of patients with sarcoma.

MSAC found that PET has a sufficiently high negative predictive value for suspected residual or recurrent disease that biopsies may be avoided in a proportion of patients when the PET scan is negative, at a modest increase in costs. MSAC noted utilisation data shows the rate of increase for this indication is high, and advised that this trend should be monitored as there is no justification for using PET for 'surveillance' of patients in the absence of clinical evidence of residual or recurrent disease.

MSAC found that in patients with newly diagnosed GIST PET detects additional sites of disease but whether this results in significant changes in management or whether this has any impact on health outcomes is highly uncertain.

MSAC also found that in patients with suspected progressive or treatment-resistant GIST PET potentially predicts response to therapy but whether this results in significant changes in management or whether this has any impact on health outcomes is uncertain. Although PET provides an early marker of disease responsiveness to imatinib, MSAC considered that clinicians should continue the current practice based on evidence from clinical trials of assessing response based on symptoms and anatomical indices of disease response, and not pre-emptively undertake surveillance with further PET scans.

8. Cost-effectiveness

MSAC noted that no studies were found showing the cost effectiveness of PET in the management of sarcoma.

Only the financial implications of funding for initial grading and guiding biopsy of suspected sarcoma and for initial staging of patients with GIST were estimated, as MSAC found that there was insufficient evidence to undertake a full economic evaluation for these indications

MSAC also found that there was insufficient evidence to undertake full economic evaluation for the evaluation of suspected residual or recurrent sarcoma after definitive treatment and for the investigation of suspected progression or treatment resistance in patients with GIST. An estimate of the main cost implications for patients with suspected residual or recurrent sarcoma was noted, and most of the data have substantial uncertainties.

A cost-consequence analysis with a decision-analytic model of patient management with and without PET was developed for initial staging of proven adult-type sarcoma, and initial staging of proven paediatric-type sarcoma.

Limited sensitivity analysis for adult-type tumours examined the effects of: frequency of unsuspected metastases detected by PET; the cost of curative surgery; and the proportion of patients in whom treatment intent changed from curative to palliative.

MSAC also noted that if public funding is approved, it is expected that utilisation would likely be higher than in the interim funding period, as PET will be offered in more centres.

9. Financial/budgetary impacts

PET is used to identify patients with more advanced disease, the results of which would change treatment intent: in patients with adult-type tumours, from curative to palliative; and for patients with paediatric-type tumours, treatment may be escalated with curative intent.

MSAC noted that direct evidence was not available, and potential health outcomes could not be quantified but were discussed qualitatively. The sensitivity analysis found that increasing the cost of curative surgery resulted in PET being associated with cost savings. The potential cost of PET to the Federal Government (assuming all costs were to be borne by the MBS) was estimated based on the potential utilisation of PET. The annual cost of PET for all sarcoma indications in Australia was calculated to be between \$1.47 million and \$3.5 million.

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

Indication 1- Initial grading and guiding biopsy of suspected sarcoma

MSAC found that the use of PET for initial grading and guiding of biopsy of sarcoma is at least equivalent to CT or MRI for the selection of an appropriate site for biopsy, but no advantage in grading could be confirmed for PET. No evidence of changes in patient management subsequent to PET was found.

Indication 2 - initial staging of biopsy proven bone or soft tissue sarcoma considered potentially curable on conventional staging (adult-type tumours)

MSAC found that the use of PET for initial staging of biopsy-proven bone or soft tissue sarcoma considered potentially curable on conventional staging more accurately detects metastases (except pulmonary metastases) in adult-type tumours. MSAC agreed the evidence base is not strong, but that PET is likely to change patient management. This would likely avoid inappropriate attempts at curative therapy (predominantly surgery) and thus improve quality of life in a proportion of those patients with more advanced disease with PET-identified additional metastases. However the magnitude of these effects and the overall impact on net costs could not be quantified.

Indication 3 - initial staging of biopsy proven bone or soft tissue sarcoma considered potentially curable on conventional staging (paediatric-type tumours)

MSAC found that the use of PET for the initial staging of biopsy-proven bone or soft tissue sarcoma considered potentially curable on conventional staging more accurately detects bone and lymph node metastases (but not pulmonary metastases) in paediatric-type tumours. MSAC agreed there was some evidence of change in patient management with the more appropriate use of escalated versus standard chemotherapy, and that this may improve disease-free or overall survival. Although the evidence base is not strong, the improved use of curative treatment is likely to have a greater impact on health outcomes in this overall younger population of patients with sarcoma.

Indication 4 - evaluation of suspected residual or recurrent sarcoma after definitive treatment

MSAC found that PET has a sufficiently high negative predictive value to result in the avoidance of biopsy in a proportion of patients when a PET scan is negative. This can potentially be achieved at a modest additional cost. MSAC noted that utilisation data show the rate of increase for this indication to be high – MSAC advised that this trend should be closely monitored as there is no justification for using PET for 'surveillance' of patients without clinical evidence of residual or recurrent disease.

Indications 5 and 6 - Initial staging of patients with newly diagnosed gastrointestinal stromal tumours (GIST) or with recurrent GIST after locoregional therapy; or investigation of suspected progression or treatment resistance in patients with GIST

MSAC found that there was a lack of clinical data and no evidence of change in clinical practice or health outcomes by performing PET/CT scanning in these indications. MSAC noted that, prior to treatment, GIST is extensively FDG avid and that this avidity rapidly reduces with successful treatment. Although PET provides an early marker of disease responsiveness to imatinib, MSAC considered that clinicians should continue the current practice based on evidence from clinical trials

of assessing response based on symptoms and anatomical indices of disease response, and not pre-emptively undertake surveillance with further PET scans. MSAC agreed that, as a result of continuing this practice, PET was unlikely to be cost saving in these indications. However, MSAC noted that these indications are the subject of current clinical trials and that cost savings may be demonstrated in the future from the use of PET scans to avoid inappropriate imatinib dose escalation or conversion to sunitinib.

11. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to the safety, effectiveness and cost-effectiveness of PET for sarcoma:

- MSAC does not support public funding for PET studies for the initial grading and guiding biopsy of suspected sarcoma. (*Indication 1*)
- MSAC supports public funding for a single whole body FDG PET/CT study performed for the initial staging of a patient with biopsy-proven bone or soft tissue sarcoma (excluding gastrointestinal stromal tumour) who is considered to be potentially curable by conventional staging methods. (*Indications 2 and 3*)
- MSAC supports public funding for a single whole body FDG PET/CT study performed for the evaluation of a patient with suspected residual or recurrent sarcoma (excluding gastrointestinal stromal tumour) after the initial course of definitive treatment to determine suitability for subsequent treatment with curative intent. (*Indication 4*) To minimise the use of repeated PET scans as surveillance in patients without clinical evidence suggestive of active disease, a use which MSAC does not support, the relevant MBS Item Descriptor should not allow more than one scan. However, MSAC advises that there is no need to prescribe a particular period of time after cessation of initial therapy before the scan is conducted.
- MSAC does not support public funding at this time for PET studies for the initial *staging* of patients with newly diagnosed *gastrointestinal stromal tumours* (GIST) or with recurrent GIST after locoregional therapy; or investigation of *suspected progression or treatment resistance* in patients with *GIST*. MSAC advises that further research is required regarding the use of PET for these indications (*Indications 5 and 6*).

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.

The MSAC Assessment Report is available at

<http://www.msac.gov.au/internet/msac/publishing.nsf/Content/Completed-References1-40>