Medical Services Advisory Committee

Public Summary Document

Reference No. 35d(i) – Positron Emission Tomography for Glioma

Sponsor: **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 the Medical Services Advisory Committee to review the value of PET using F-18 fluorodeoxyglucose (FDG) for:

1. Initial ***diagnosis*** of malignancy in primary brain tumour (MRI equivocal for malignancy);
2. ***Grading*** of glioma (indeterminate grade on MRI):triage prior to biopsy; and
3. Assessment of ***suspected residual / recurrent glioma***

2. Current arrangements for public reimbursement

The MBS interim funding arrangement (Item number 61538), due to cease on 1 July 2010, provides reimbursement for FDG PET study of the brain performed for the evaluation of a residual structural brain lesion based on anatomical imaging findings, after definitive therapy for glioma.

3. Background

PET is a nuclear imaging technique using a short lived radiopharmaceutical (in this instance 2-^{18}F-fluoro-2-deoxy-D glucose, FDG). The technique provides functional and metabolic information and current scanners incorporate CT (but not MRI) in the same instrument. In the case of brain tumours, FDG PET/CT is usually complemented by anatomical imaging with magnetic resonance imaging (MRI).

Primary tumours of the brain and central nervous system (CNS) are uncommon, heterogenous and biologically complex, reflecting the diversity of cell types within the brain. Their pathological classification is also complex, but can be broadly divided into tumours derived from glial cells, neuronal cells, cells that surround or insulate the CNS, and cells that form specialised anatomic

structures. The frequency of individual tumour types roughly reflects the frequency and proliferative capacity of cell types. While neuronal cells become largely post-mitotic after development, glial cells retain the ability to proliferate, and gliomas are therefore the most common type of brain tumour. Glial cells that are thought to give rise to specific tumour types include astrocytes (astrocytomas), oligodendrocytes (oligodendrogliomas) and ependymal cells (ependymomas).

High-grade gliomas typically have increased glucose metabolism relative to normal white matter, while low-grade tumours have relatively reduced glucose metabolism compared to normal cerebral cortex and similar or slightly higher metabolism than normal white matter.

FDG PET can be used to identify regions of increased glucose metabolism to guide biopsy and resection, differentiate high-grade from low-grade tumours, detect malignant degeneration in low-grade gliomas, and also to separate recurrent tumour from the effects of treatment (e.g., radiation necrosis).

4. Clinical need

MSAC noted that primary brain tumours are relatively rare – some 1.4% of all new cases of cancer, i.e. 1,422 new cases in 2005 in Australia. Gliomas accounted for 2.7% of all cancer deaths in 2005.

5. Comparator

MSAC acknowledged the comparator as follows:

1. In patients with suspected primary brain tumours the comparator is the addition of PET to MRI (when MRI is equivocal for malignancy).
2. For tumour grading, the assessment report compares the addition of PET to MRI when MRI is positive for malignancy, but with indeterminate grade, as a triage to subsequent biopsy.
3. For evaluation of patients with suspected residual or recurrent brain tumour, PET is directly compared with biopsy or surgical excision, or compared with serial MRI or CT when surgery is delayed.

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

No direct evidence was found comparing outcomes of patients with brain tumours managed with or without PET. Linked evidence was used to determine accuracy, change in management and benefits of changes in treatment to evaluate effectiveness of PET.

PET in the initial diagnosis of patients with suspected primary brain tumour

PET was found to detect malignancy in up to one third of patients with primary brain tumours. However, the incremental value of PET over MRI, the changes in management associated with PET findings and their resultant impacts on health outcomes were uncertain.

PET for tumour grading in patients with primary brain tumour

A negative PET scan was found to be only modestly predictive of the absence of high-grade disease and no studies evaluated patients with indeterminate grading on prior tests or the therapeutic impact of PET grading. Changes in patient management associated with these findings are unknown, but are expected to be infrequent.

PET for detection of residual or recurrent brain tumour

MSAC noted PET was found to be predictive of the presence of residual or recurrent disease when the PET scan is positive, and the absence of residual or recurrent disease when the PET scan is negative.

MSAC found that there was evidence that PET leads to changes in patient management, including a change in a small number of patients from observation to surgery and/or chemotherapy, and a change from surgery to non-surgical management.

MSAC noted that PET was likely to lead to improvements in patient outcomes when inappropriate surgery is avoided and when surgery and/or chemotherapy is appropriately initiated. The magnitude of this effect has not been quantified. MSAC also noted that PET may lead to an increase in costs, associated with a benefit of uncertain magnitude.

8. Cost-effectiveness

MSAC noted there was insufficient evidence to undertake an economic evaluation for the use of PET in initial diagnosis of patients and for tumour grading in patients with primary brain tumour.

However, a cost consequence analysis was used to estimate the cost of PET for assessment of suspected residual/recurrent malignancy. For this indication the incremental cost of PET was $63,000 per 100 patients. MSAC noted in a small number of patients, PET resulted in more appropriate initial surgery, chemotherapy, and/or more frequent clinical observation of patients with untreatable disease.

However, MSAC also noted that the modelled use of PET does not reduce the frequency of unnecessary initial surgery, and may occasionally lead to a delay in undertaking appropriate surgery and/or may lead to the inappropriate initiation of chemotherapy.

MSAC observed that a threshold analysis identified that PET would become cost-saving when prevalence in those undergoing observation increased to 52%. All other scenarios showed incremental costs for PET.

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

On balance, MSAC found that FDG PET has sufficient accuracy for detecting and ruling out residual/recurrent malignancy and is likely to lead to more appropriate management in a significant proportion of patients, which in turn is likely to improve patient outcomes. MSAC judged that these unquantified improvements justify the costs of PET in this setting.

9. Financial/budgetary impacts

The cost to the MBS for the detection of residual or recurrent disease, was estimated to be between $291,000 and $537,900 per annum. For all glioma indications, it is estimated to be between $658,600 to $1,738,900 annually.

The benefits associated with the change in patient management were not quantified, but discussed qualitatively.

Resource costs were calculated using a whole of healthcare perspective. The modelled analysis shows total costs in the PET arm of $1,170,300 per 100 patients, compared with $1,107,300 in the non-PET arm, resulting in incremental costs in the PET arm of $63,000 per 100 patients.

MSAC acknowledged that cautious interpretation of these costings was required as there was considerable uncertainty around the estimates.

MSAC found the main economic areas of uncertainty were in the model inputs, and the unknown proportion of public versus private utilisation of PET should public funding be approved.

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

MSAC considered the utilisation of PET for glioma in Australia, and agreed there need to be better

treatments and diagnosis available for this disease.

MSAC agreed that PET was safe in all proposed glioma indications, but there was insufficient evidence to support public funding for the initial diagnosis of patients with suspected primary brain tumour in whom MRI is equivocal for malignancy, or for tumour grading in patients with glioma in whom MRI grading is indeterminate. For initial diagnosis, PET was able to detect malignancy in up to one-third of patients with primary brain tumours; however, the incremental value of PET over MRI, changes in management associated with PET findings and their resultant impacts on health outcomes were uncertain. For tumour grading, PET was found to be only modestly predictive of the absence of high grade disease when the scan was negative, and no studies evaluated patients with indeterminate grading on prior tests or the therapeutic impact of PET grading.

However, MSAC agreed to support public funding for PET for detection of residual or recurrent malignant brain tumour because FDG PET has sufficient accuracy for detecting and ruling out residual/recurrent malignancy and is likely to lead to more appropriate management in a significant proportion of patients, which in turn is likely to improve patient outcomes. MSAC judged that these unquantified improvements justify the costs of PET in this setting.

MSAC acknowledged that the body of evidence was limited, but that a better evidence base for FDG PET was unlikely in the foreseeable future.

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 in glioma:

- MSAC supports public funding for a single FDG PET/CT study of the brain performed for the evaluation of a patient with suspected residual or recurrent malignant brain tumour on anatomical imaging after definitive therapy (or during ongoing chemotherapy) who is considered to be a candidate for further active treatment.
- MSAC does not support the public funding of PET studies for the initial diagnosis of patients with suspected primary malignant brain tumour.
- MSAC does not support the public funding of PET studies for tumour grading in patients with malignant brain tumour.

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