



Medical Services Advisory Committee

Public Summary Document

Reference No. 35e – Positron Emission Tomography for Cervical Cancer

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 Schedule (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 assessing:

1. patients with locally advanced, potentially curable cervical cancer (ie stage \geq IB2) for *staging* of disease
2. patients with *suspected* local recurrence of cervical cancer
3. patients with *confirmed* local recurrence of cervical cancer, considered potentially curable on conventional staging

2. Current arrangements for public reimbursement

The MBS interim funding arrangement, due to cease on 1 July 2010, provides reimbursement for whole-body FDG-PET performed for the primary staging of proven carcinoma of the uterine cervix, before planned radical radiation therapy or combined modality therapy (with/without catheterisation of the bladder).

The MBS item descriptors for these interim funded items are:

61571 Whole body FDG PET study, performed for the primary staging of proven carcinoma of the uterine cervix, prior to planned radical radiation therapy or combined modality therapy.

61574 Whole body FDG PET study, performed for the primary staging of proven carcinoma of the uterine cervix, prior to planned radical radiation therapy or combined modality therapy, with catheterisation of the bladder.

3. Background

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

The main role of PET both in the initial staging of locally advanced cervical cancer and in the assessment of confirmed local recurrence (both considered potentially curable on conventional staging) is to detect distant metastases. This information will influence whether treatment should be offered with curative or palliative intent. As a consequence some patients may avoid the morbidity and mortality associated with treatments usually reserved for individuals who have potentially curable disease. On the other hand, PET may provide reassurance that curative treatment is appropriate. Despite these theoretical advantages, there are no published clinical trials comparing treatment of patients with disseminated metastatic disease detected only by PET. Thus it is not known whether the potential improvement in quality of life through avoiding the morbidity associated with inappropriately aggressive treatment outweighs any potential benefit of such treatment.

4. Clinical need

MSAC considered the trends of the incidence rates of cervical cancer over the last three decades in Australia. MSAC also considered the proportion of patients falling into the three categories, namely initial staging and evaluation of confirmed and suspected local recurrence.

MSAC noted that cervical cancer is mainly caused by human papilloma virus (HPV) and that the incidence of cervical cancer (in particular squamous cell) has fallen significantly since the establishment of the National Cervical Cancer Program in the early 1990's. The rates have now plateaued and it is unlikely that incidence will change substantially from the 2006 rates (715 incident cases and rates of 6.6 per 100,000) in the next five years as a result of the National Screening program. It was also noted that the decrease in incidence of adenocarcinoma was not as marked as the decrease in squamous cell cancer and that it was reasonable to assume that there will be no further decreases in adenocarcinoma due to screening. The recent addition of HPV vaccination to the National Immunisation Program (NIP) Schedule would only be expected to have a very small impact on the rates of cervical cancer, at least in the next 5 years. There was no evidence that the distribution of cervical cancer at diagnosis is likely to change over the short term (approximately 65% localised disease, 15% regional and 17% metastatic). MSAC also noted that curative treatments include surgery, standard or extended field chemo-radiation and palliative treatments.

MSAC also noted data collected from Australian centres using PET for cervical cancer during the interim funding period.

5. Comparator

MSAC agreed that the appropriate comparators for the role of PET scanning are CT and MRI scanning as prior tests. MSAC noted that, prior to PET/CT scanning, most patients will have had diagnostic CT scans as part of their routine staging work-up, and some will also have had MRI scans for better definition of local (particularly parametrial) extent of disease.

6. Safety

MSAC noted that 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 for this patient group.

7. Clinical effectiveness

Indication 1 - Initial staging of locally advanced potentially curable cervical cancer

MSAC agreed that the use of PET/CT for the initial staging of locally advanced potentially curable cervical cancer leads to appropriate upstaging of some patients, however the extent to which this occurs is uncertain. MSAC noted that there was no evidence presented to support the claim that upstaging results in the delivery of treatment which would improve overall survival. The application outlined a pathway whereby upstaging identified para-aortic lymph node involvement which would potentially result in extension of the radiation treatment fields. No evidence was presented that extended field radiotherapy for patients with para-aortic lymph node involvement improved survival, although it was noted that this treatment reflects current practice.

Indication 2 - Suspected (unconfirmed) local recurrence

PET/CT was considered by MSAC to be likely to increase the accuracy of detection of additional disease sites and may obviate the need for invasive procedures or unnecessary treatment in patients with disseminated disease, but the extent to which PET leads to changes in management was uncertain. The impact of PET on health outcomes was uncertain and cost consequences were unknown.

Indication 3 - Confirmed local recurrence

Based on extrapolation from other diseases, it is plausible that salvage chemoradiation or pelvic exenteration may cure a small number of highly selected patients. PET/CT was considered by MSAC to increase the accuracy of detection of additional disease sites (i.e., locoregional extent or distant metastases) not suspected on prior tests and to be likely to lead to a change in management intent from curative to palliative treatment in about one third of patients. PET/CT was therefore likely to lead to improved patient outcomes when inappropriate aggressive therapy such as radical surgery (pelvic exenteration) that is unlikely to be curative is avoided, and initiating palliative therapy is likely to improve quality of life for the patient.

8. Cost-effectiveness

MSAC noted that with regard to the measurement and magnitude of clinical benefit, economic analysis was restricted to patients with confirmed local recurrence (indication 3) and may lead to improved quality of life by avoiding inappropriate treatment with curative intent, but quality of life changes could not be quantified.

9. Financial/budgetary impacts

MSAC noted that a modelled economic evaluation was not undertaken due of the paucity of data. Instead, an estimate of the major cost implications was undertaken of PET in patients with confirmed local recurrence of cervical cancer.

MSAC agreed that the potential size of patient population that would use the service might range from 410 to 476 PET examinations per year but may be greater if the number of sites is expanded and/or there is no limit placed on the number of scans.

MSAC note that at a unit cost of \$953, the gross cost to Commonwealth Government is in the range \$391,000 - \$454,000 per year with no allowance for patient co payment in this estimate.

MSAC's main economic concerns or areas of uncertainty were around: whether PET/CT scans were to be used in addition to conventional imaging or as a substitute, and if as a substitute whether PET/CT could be cost-saving; and whether there was potential for leakage through the use of PET/CT for disease surveillance.

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

Indication 1 - Initial staging of locally advanced potentially curable cervical cancer

MSAC agreed that the use of PET/CT for the initial staging of locally advanced potentially curable cervical cancer leads to appropriate upstaging of some patients, but the extent to which this occurs is uncertain. MSAC noted that there was no evidence presented to support the claim that upstaging results in the delivery of treatment which would improve overall survival. The application outlined a pathway whereby upstaging identified para-aortic lymph node involvement which would potentially result in extension of the radiation treatment fields. No evidence was presented that extended field radiotherapy for patients with para-aortic lymph node involvement improved survival, although it was noted that this treatment reflects current practice.

Indication 2 - Suspected (unconfirmed) local recurrence

MSAC agreed that there was insufficient evidence to support public funding for this indication. Although PET could detect sites of suspected local recurrence not identified by CT or MRI, the extent to which this would lead to changes in management or improvements in health outcomes was uncertain.

Indication 3 - Confirmed local recurrence

MSAC agreed that evidence of clinical benefit was largely confined to this indication. MSAC agreed that the detection of metastatic disease will change the intent of therapy from potentially curative to palliative in about one third of patients with confirmed local recurrence. Although the impact of this diagnostic information on local therapies and health outcomes has not been satisfactorily quantified, avoiding aggressive therapy such as radical surgery that is unlikely to be curative, and initiating palliative therapy, is likely to improve quality of life for the patient.

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 cervical cancer:

- MSAC supports public funding for a single whole body FDG PET/CT study performed for the further primary staging of a patient with histologically-diagnosed carcinoma of the uterine cervix, at FIGO stage IB2 or greater by conventional staging, prior to planned radical radiation therapy or combined modality therapy with curative intent. (*Indication 1*)
- MSAC does not support public funding of PET studies for suspected local recurrence of cervical cancer. (*Indication 2*)
- MSAC supports public funding for a single whole body FDG PET/CT study performed for the further staging of a patient with confirmed local recurrence of carcinoma of the uterine cervix who is a candidate for salvage pelvic chemoradiotherapy or pelvic exenteration with curative intent. (*Indication 3*)

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 [*link when published and agreed by Minister to publicly release outcomes*].