

# Medical Services Advisory Committee (MSAC) Public Summary Document

## ***Application No. 1562 – Streamlining Medicare Benefits Schedule Items for Positron Emission Tomography (PET) Project***

**Applicant:** Department of Health and Aged Care

**Date of MSAC considerations:** 30-31 March 2023  
25-26 November 2021  
29 July 2021  
28-29 November 2019

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website](#).

### **1562 – Streamlining Medicare Benefits Schedule (MBS) items for PET Project: assessment of treatment response and suspected recurrence**

**Date of MSAC consideration:** 30-31 March 2023

#### **MSAC’s advice to the Minister – March 2023**

After considering the strength of the available evidence in relation to comparative safety, clinical effectiveness, cost-effectiveness and total cost, MSAC supported the creation of a new Medicare Benefits Schedule (MBS) item for assessment of treatment response and recurrence by fluorodeoxyglucose positron emission tomography (FDG-PET) in patients with rare or uncommon cancers. MSAC acknowledged the clinical need for the proposed testing in this population. MSAC considered that FDG PET has a well-established safety and effectiveness profile, being a more accurate technique for characterising disease and thereby improving patient management compared with conventional imaging. MSAC noted the limitations in the costing analysis, but considered that that FDG PET would have an acceptable budget impact. MSAC also noted that FDG PET is the standard of care in this patient population.

The MSAC supported item descriptor is provided below:

Category 5 – Diagnostic Imaging Services
Item 616xx
Whole body FDG PET study, following initial therapy, performed for the evaluation of suspected residual, metastatic or recurrent cancer for a patient who is undergoing or is suitable for active therapy, if the eligible cancer type is:  (a) a rare or uncommon cancer (<12/100,000/year); and  (b) a typically FDG-avid cancer.
Fee: \$953.00                      Benefit: 75% = \$714.75 85% = \$859.80

## Consumer summary – March 2023 MSAC consideration

This is an application from the Department of Health and Aged Care requesting Medicare Benefits Schedule (MBS) listing of a specific type of scan in patients being treated for certain rare or uncommon cancers. The full name of the scan is [<sup>18</sup>F]fluorodeoxyglucose positron emission tomography/X-ray computed tomography imaging. In this summary, it is referred to as an FDG PET study. This application arose from a Department of Health project that was originally started because of the limited evidence available to conduct conventional health technology assessments to evaluate FDG PET/CT across all cancer types and for all purposes.

FDG stands for fluorodeoxyglucose, which is a mildly radioactive type of sugar that is injected into the patient's body as a tracer. PET stands for positron emission tomography, which is a medical imaging technique. X-ray computed tomography (CT) imaging uses special X-ray equipment to produce images of the inside of the body. A combined PET/CT scanner can do both PET and CT scans at the same time, which helps doctors to more accurately detect and define cancers.

Some cancers take up FDG, which means that they show up as bright spots on the scan. Doctors can then decide how advanced the cancer is (called "staging"). Staging helps doctors decide on the best course of treatment for the patient.

MSAC previously supported MBS listing of FDG PET/CT for initial staging for a set of rare or uncommon cancer types. This became available as MBS item 61612 in November 2022. The list of rare or uncommon cancers is available online in the associated notes for item 61612<sup>1</sup>. This application asked MSAC to support a new MBS item for FDG PET/CT for assessment of treatment response and restaging (when the cancer is staged after the initial staging) of the same set of cancers, after treatment has begun. This way, it can be used to check if the cancer has returned (recurrent cancer).

MSAC noted FDG PET/CT to be the current standard of care in oncology because it more accurately defines the extent of disease compared with conventional (other types of) medical imaging.

### MSAC advice to the Commonwealth Minister of Health and Aged Care

MSAC supported listing the new item for FDG PET/CT for the assessment of treatment response and suspected recurrence in patients with certain rare or uncommon cancers. MSAC considered that FDG PET/CT has well established safety and effectiveness compared with conventional imaging. MSAC also considered that that FDG PET would have an acceptable budget impact. MSAC noted that the MBS Review had recommended this item be created.

## Summary of consideration and rationale for MSAC's advice – March 2023

MSAC noted that the purpose of this submission is to expand MBS funding of [<sup>18</sup>F]fluorodeoxyglucose positron emission tomography/X-ray computed tomography imaging (FDG PET/CT) for assessment of treatment response and suspected recurrence of rare or uncommon cancers that meet certain qualification criteria.

MSAC recalled that this application is part of a project to review use of FDG PET/CT for rare cancers, as recommended by the MBS Review Taskforce. Rare or uncommon cancers were

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<sup>1</sup> <http://www9.health.gov.au/mbs/fullDisplay.cfm?type=item&qt=ItemID&q=61612>

defined as those with an annual incidence of less than 12 per 100,000 person-years. A PET Working Group has been meeting since 2018 and carrying out this work in phases:

- Phase 1 – The Working Group developed and tested a generic economic model (GEM) and a matrix to estimate the proportion of patients who would need FDG PET/CT for initial staging, the proportion of patients whose management would change as a result, and the expected cost to the MBS.
- Phase 2 – MSAC supported listing of FDG PET/CT to identify and stage a list of rare or uncommon cancer types where these studies change the patient's management. [MBS item 61612](#) became available in November 2022; the associated notes list 26 cancer types that are considered rare or uncommon. These cancers comprise a third of all cancer diagnoses.
- Phase 3 (current application) – MSAC to consider MBS funding for progress FDG PET/CT to assess both response to treatment and recurrence in these rare or uncommon cancers.

MSAC recalled that the MBS Review Taskforce had recommended that access be expanded to all FDG-avid cancers for staging and progress assessment for four indications: diagnosis, staging, response to therapy and recurrence. MBS item 61612 covers diagnosis and initial staging of these rare or uncommon cancers and this proposed item will cover response to therapy and recurrence.

MSAC acknowledged the clinical need for the proposed testing in this population.

MSAC noted that the MSAC Executive had reviewed the clinical management algorithm showing the place of initial and repeat FDG PET/CT in the management of the proposed population. In some cases, FDG PET/CT will replace other types of conventional imaging such as CT scan or MRI scan; in others, it will augment other scans. MSAC agreed that the clinical management algorithm could be used as the basis for determining the scope of a FDG PET/CT MBS item for treatment response and cancer recurrence.

Under this proposed item, patients must be referred by a specialist or consultant physician. Providers of services under the proposed item will be as per item 61612, namely medical specialists who are recognised as appropriate providers of PET by the MBS. MSAC reviewed and supported the draft item descriptor and fee as presented.

MSAC accepted Departmental advice that there should not be an annual restriction on the number of FDG PET/CT studies a patient can have, as the number of scans required to assess response to therapy or recurrence will vary across cancer types and individuals. MSAC also considered there should not be any restriction on other forms of imaging being claimed for the same patient, as patients may initially have a CT scan and later need a PET scan. The referring specialist will decide which type of scan is required.

MSAC advised that consumers and stakeholders should be consulted as part of the implementation process for this item, to ensure their perspectives are considered.

MSAC noted that it has previously accepted the clinical effectiveness and safety profile of FDG PET/CT and considered them to be acceptable for the initial staging of these rare or uncommon cancers – so it was logical to extend this conclusion to the use of FDG PET/CT for restaging and progress assessment of the same cancers. This is because FDG PET/CT more accurately defines the extent of disease compared with conventional imaging for the identified list of rare or uncommon cancers and this in turn leads to improved treatment allocation. MSAC also noted that FDG PET/CT is the standard of care imaging modality in oncology.

MSAC noted that it was not possible to obtain high-level Australian cost-effectiveness data on each rare cancer, as the numbers of patients are too low. MSAC recalled that the Working Group

had previously developed a matrix to model the potential use of FDG PET/CT for initial staging, and estimate its likely cost to the MBS budget. The PET Working Group then extended the matrix to include assessment of treatment response and evaluation of suspected recurrence. The matrix assessed the likely need for FDG PET/CT during the management of 26 rare or uncommon cancers, either after locoregional therapy (with curative intent) or during systemic therapy.

MSAC agreed with the MSAC Executive and supported the combination of matrix data and MBS data as a reasonable basis to estimate the cost of this listing.

MSAC noted the financial analysis was estimated from several sources of information:

- The matrix with clinical experts' (oncologists) estimates of the proportion of patients with each selected cancer type who are likely to require FDG PET/CT to evaluate recurrence or to assess response to therapy, and consequent changes in management.
- MBS data of PET use in the first 5 years after diagnosis in other common cancers (colorectal cancer, ovarian cancer and lymphoma)
- Drug Utilisation Sub-Committee (DUSC) linkage of MBS and PBS data in lymphoma.

The financial analysis used these data to estimate the financial impact to the MBS for two groups of patients. "Incident" patients are those who have their first progress scan in a given year. "Prevalent" patients had their first scan before that year and require further progress scans in the given year. The analysis showed that the estimated net financial impact to the MBS for expected scan use by both incident and prevalent patients was \$14.8 million in the first year, increasing to \$18.4 million in the fourth year. MSAC considered that the incremental cost to the MBS due to funding this application is likely to be relatively modest.

MSAC noted that both MBS and DUSC data showed that ongoing use of PET decreases significantly from the first year into the second year, and continues to decline rapidly in subsequent years. The average number of follow-up PET services is less than two per patient per year.

MSAC recalled that the estimated cost for FDG PET/CT scans for initial staging (under MBS item 61612) was \$13 million a year, and that this item had been tracking lower than estimated in its first 4 months of listing. MSAC considered the estimated costs for the current application to be acceptable and noted that they are likely to be an overestimate. This is because the model assumes that every patient who is eligible will be scanned under Medicare, and it does not include potential savings that will result from patients avoiding unnecessary therapies.

MSAC acknowledged that this application is supported by a financial analysis rather than an economic evaluation. Although normal practice is for MSAC to require an economic evaluation, it was problematic to employ an economic evaluation in this case as there are not enough data to allow a cost-effectiveness analysis for each rare cancer. For more common cancers, real-world MBS utilisation data and cost-effectiveness data are available, but this is not the case for rare cancers. MSAC had therefore agreed to a different approach for the PET Project, which was focused only on FDG-avid cancers. MSAC recalled that, in June 2021, ESC had supported piloting the GEM approach to assess FDG PET/CT in rare or uncommon cancer types. This had been tested with two validation studies and five case studies. At its November 2021 meeting, MSAC accepted that the GEM provides a pragmatic way forward for assessing funding for staging of rare or uncommon cancer types. MSAC continues to require cost-effectiveness analyses with applications whenever the data allow.

## **Other matters**

MSAC discussed the next steps for the PET streamlining project, and accepted the Department's proposal to consider how to extend the streamlined FDG PET approach to cover more common cancers. MSAC also discussed the Department's proposal to convene a similar working group for

MRI, made up of different experts. The MRI Working Group will consider how best to incorporate the wider use of MRI for rare or uncommon cancers into the MBS. MSAC noted the Department's belief that that current streamlining project has produced a useful methodology which can be applied by the MRI working group. MSAC advised that the MRI Working Group should continue to involve consumer representatives.

**1562 – Streamlining Medicare Benefits Schedule items for PET Project: initial staging of rare or uncommon cancer types**

**Date of MSAC consideration: 25-26 November 2021**

**MSAC's advice to the Minister – November 2021**

MSAC supported the creation of a new Medicare Benefits Schedule (MBS) item for initial staging by fluorodeoxyglucose positron emission tomography (FDG-PET) of rare or uncommon cancer types meeting certain qualification criteria. MSAC accepted that these qualification criteria had been validated through the development of a generic economic model and had identified cancer types likely to result in a significant change in management for those patients with a resulting change in staging. MSAC also acknowledged the budget impact of limiting the MBS item to the eligible cancer types.

**Consumer summary – November 2021 MSAC consideration**

The positron emission tomography (PET) Project was started because of the limited evidence available to conduct conventional health technology assessments to evaluate FDG PET/CT across all cancer types and for all purposes (such as staging, which means working out how large a tumour is and how far it has spread). There are approximately 200 rare or uncommon cancer types, which together comprise 30% of all diagnosed cancers. However, when only a small number of people have a specific type of cancer, it is difficult to get enough evidence to make decisions about safety, clinical effectiveness, cost-effectiveness and financial impacts.

PET is a type of imaging test, which means it is used to look inside the body to diagnose and assess diseases such as cancer. A radioactive substance commonly used in PET scanning is FDG (fluorodeoxyglucose). After radioactive FDG is injected into the bloodstream of a patient, a PET scanner can form two-dimensional or three-dimensional images of the distribution of FDG within the body. An FDG-PET scan is often used with computed tomography (CT) to help radiologists tell the difference between healthy tissue and diseased tissue. This way, cancer can be accurately diagnosed, correctly staged and appropriately treated.

The first phase of this Project was to look at FDG PET/CT for initial staging of rare or uncommon cancer types. The PET Working Group of MSAC helped to develop a generic economic model (GEM) to identify those cancer types likely to result in a significant change in management as a result of being more accurately staged using FDG PET/CT.

The PET Working Group advised that it may be possible to extend the "triage criteria" that were developed to select cancer types to be assessed using the GEM. Other rare or uncommon cancer types were then selected to assess these extended criteria with reference to the GEM. This enhanced set of criteria then became the proposed qualification criteria to identify those rare or uncommon cancer types for which MSAC could support funding for FDG PET/CT for initial staging.

The PET Working Group applied the proposed qualification criteria to the Australian Institute of Health and Welfare list of rare or uncommon cancer types and identified 23 cancer types in which FDG PET/CT for initial staging is likely to be clinically effective and cost-effective.

### **MSAC's recommendation to the Commonwealth Health Minister**

MSAC supported the creation of a new Medicare Benefits Schedule (MBS) item for initial staging by fluorodeoxyglucose positron emission tomography (FDG-PET) of rare or uncommon cancer types that meet certain qualification criteria.

MSAC accepted that these qualification criteria had been validated through the development of a generic economic model. MSAC also acknowledged the budget impact of limiting the MBS item to the eligible cancer types.

### **Summary of consideration and rationale for MSAC's advice – November 2021**

MSAC noted that the current extent of Medicare Benefits Schedule (MBS) funding for positron emission tomography/computed tomography (PET/CT) use is relatively small compared to the current extent of clinically accepted use. As part of the MBS Review, the Diagnostic Imaging Clinical Committee recommended use of four clinically based, cancer-agnostic indications for MBS funding of fluorodeoxyglucose positron (FDG) PET/CT: diagnosis, staging, response assessment, and re-staging for suspected residual or recurrent cancer. The PET Project was initiated in recognition of the limited resources and availability of relevant evidence to conduct conventional health technology assessments to evaluate FDG PET/CT across all cancer types and across all purposes. The initial focus of the Project was initial staging of rare or uncommon cancer types, which collectively account for 30% of new cancer diagnoses, and for which an initial set of five eligibility criteria were established to triage the cancer types to be assessed.

MSAC recalled the outcomes from the July 2021 MSAC meeting:

- The decision to truncate the time horizon of the generic economic model (GEM) to 12 months was necessary to reduce modelling complexity, but it reduced the capacity of the model to fully capture net health gains attributable to changes in treatment options.
- For the seven cancer types explored with the GEM, MSAC accepted ESC's advice to interpret the incremental cost per improved treatment allocation decision alongside the 12-month incremental cost per quality-adjusted life year (QALY).
- More work was required to understand (qualitatively) the drivers of the GEM, such as life expectancy without improved treatment and life expectancy gained with improved treatment.
- More clarity on the interrelationships between the model drivers should allow the elucidation of qualification criteria that would discriminate between cost-effective and cost-ineffective uses of FDG PET/CT for initial staging.

As a result of the July 2021 MSAC meeting, MSAC noted that the PET Working Group:

- explored ways to extend the original "triage criteria" to develop "qualification criteria", including a definition of management change that is identical to that used in previous MSAC Reviews that supported MBS funding of FDG-PET for colorectal, head and neck, ovarian, and oesophagogastric cancer, and for melanoma, sarcoma, and lymphoma
- applied the proposed qualification criteria to the 36 rare or uncommon cancer types listed by the Australian Institute of Health and Welfare (including the five case studies originally explored)
- identified 23 cancer types (including those used for the five case studies) in which FDG PET/CT for initial staging is likely to be clinically effective and cost-effective.

MSAC noted that it had been requested to advise on whether the proposed qualification criteria are acceptable and to determine the next phase of the Project.

MSAC accepted the proposed qualification criteria, with minor amendments (deleted text marked as strikethrough and additional text in bolded italics):

- the cancer type is ~~typically~~ ***normally expected to be*** <sup>18</sup>FDG-avid;
- the annual incidence of the cancer type meets the definition of rare or uncommon (<12 per 100,000 person-years);
- there are different clinical treatment options available for that cancer type, the selection of which is affected by whether the initial staging with FDG PET/CT has identified either distant metastases or evidence of the cancer in regional lymph nodes;
- there is ~~a sufficient proportion~~ ***at least 10%*** of patients with that cancer type for whom the initial staging FDG PET/CT result will inform a significant change in clinical management;
- there is clear basis to conclude that the resulting change in the clinical management would be characterised as
  - improving the net health outcomes for the patients receiving the change in management to a *sufficient* extent; OR
  - reducing the costs of related healthcare resources to a *sufficient* extent (up to and including generating net healthcare resource savings); OR
  - both improving the net health outcomes for the patients receiving the change in management and reducing the costs of related healthcare resources to a *sufficient* extent.

MSAC questioned whether “sufficient” in the 5th dot point (highlighted in italics) is the most appropriate word, or whether it needed to be more specific.

MSAC questioned if initial staging should occur at the beginning of a patient’s clinical management pathway or if it should be reserved for a later point. MSAC decided to leave the wording of the descriptor as “initial staging” of eligible cancer types, rather than adding in “newly diagnosed” to provide flexibility in timing. MSAC acknowledged that, for some cancer types, the initial staging might be better done later in the course of treatment. It would be up to requester when in the patient pathway to perform FDG PET/CT. MSAC questioned whether removing “newly diagnosed” might risk initial staging being misinterpreted as allowing restaging, but was reassured that the proposed item descriptor is limited to once per cancer diagnosis.

MSAC considered that “at least 10%” expectation of a change in clinical management is reasonable and noted that the oncologists consulted had advised that it is unlikely less than 10% of patients with an eligible cancer type would experience a treatment change. MSAC noted that the PET Working Group, which had sought expert oncological opinion on these estimates, noted that even when FDG PET/CT is only relevant for a small number of patients with an eligible cancer type, the proportion expected to experience a change in their management is substantial.

MSAC noted the PET Working Group also completed a matrix that was used to assess which cancer types would potentially meet the proposed qualification criteria for FDG PET/CT for initial staging. As part of this exercise, clinical experts estimated the proportion of patients in each selected cancer type who are likely to require FDG PET/CT for initial staging. Clinical experts also estimated the proportion of these patients for whom FDG PET/CT is likely to provide an effective change of management.

The PET Working Group reviewed the inputs into the matrix and concluded that FDG PET/CT for initial staging would provide effective change management for the following 23 rare or uncommon cancer types:

- anal cancer
- bladder cancer

- brain and other central nervous system (cancer of the)
- brain cancer
- gallbladder and extrahepatic bile ducts (cancer of the)
- gastrointestinal stromal tumours (GIST)
- Kaposi sarcoma
- liver cancer
- Merkel cell cancer
- mesothelioma
- ovarian cancer (incidence only)
- ovarian cancer and serous carcinomas of the fallopian tube
- pancreatic cancer
- penile cancer
- peritoneal cancer
- placenta cancer
- small intestine (cancer of the)
- stomach cancer
- testicular cancer
- unknown primary site (cancer of)
- uterine cancer
- vaginal cancer
- vulvar cancer.

MSAC expressed some doubt about the inclusion of GIST given the unfavourable results of the GEM for this case study, which was based on assuming all patients with GIST would be initially staged with FDG PET/CT, whereas clinical practice is to select only a low proportion of patients with GIST for whom FDG PET/CT would be needed. Overall, MSAC supported its inclusion for consistency of approach with the other 22 identified cancer types.

MSAC noted that cervical cancer, tongue cancer, mouth cancer, lip cancer, major salivary gland cancer and bone cancer also meet all the proposed qualification criteria. However, the MBS already funds FDG PET/CT for patients with these cancer types, so MSAC considered that there was no need to include them in the proposed MBS item.

MSAC noted that the following cancer types meet the criteria for “rare or uncommon” and “FDG-avid”, but are insufficiently defined for further assessment and thus possible inclusion in the proposed MBS item:

- other and ill-defined digestive organs
- other female genital organs excluding serous carcinomas of the fallopian tube
- other male genital organs
- other endocrine glands
- other CNS cancers
- other thoracic and respiratory organs
- other and ill-defined sites.



MSAC noted that the maximum potential cost to the MBS, if all 23 cancer types that met the “eligibility criteria” were listed, would be approximately \$9.3 million per year. In summary, MSAC concluded that, despite being limited to a 12-month timeframe, the GEM provided a sound basis for developing and assessing qualification criteria whereby using FDG PET/CT for initial staging could be supported for 23 additional rare or uncommon cancer types.

MBS therefore supported the proposed MBS item below.

<b>CATEGORY 5 – DIAGNOSTIC IMAGING SERVICES</b>	
Item number TBA	Group 14 - Nuclear Medicine Imaging Subgroup 2 - PET
Whole body FDG PET study for the initial staging of <del>newly diagnosed</del> eligible cancer types, for a patient who is considered suitable for active therapy.	
Where an eligible cancer type is:	
(a) a rare or uncommon cancer (<12/100,000/year); and	
(b) normally expected to be an FDG-avid cancer.	
Where there is at least a 10% likelihood that the PET study result will inform a significant change in management for the patient.	
Once per cancer diagnosis	
Fee: \$953.00	

Explanatory note rather than in the item descriptor to list the 23 additional eligible cancer types.

MSAC considered what would happen to those cancer types where there is insufficient information available on the change in clinical management, and what would happen if clinical management changes and more information becomes available. How would they be added on the MBS item? To address this, MSAC decided to list eligible cancer types in the explanatory notes, to allow anyone to approach the Department of Health if they believe that their cancer type could meet the qualification criteria. The HTA and policy areas of the Department could then provide an initial assessment against the criteria for consideration by the MSAC Executive. If supported, then the cancer type could be added to the list in the explanatory note.

MSAC discussed issues regarding whether the GEM approach could be:

- used to evaluate FDG PET/CT for the initial staging of FDG-avid common cancer types for which it is not currently MBS funded
- modified to evaluate FDG PET/CT for the subsequent uses (restaging, response assessment and/or monitoring) of FDG-avid rare or uncommon cancer types for which it is not currently MBS funded.

MSAC noted that FDG PET/CT is a mature technology and currently the HTA process is complex. As such, the original aim of the PET Project was to try to simplify this process, focussing first on initial staging, then restaging and then treatment response (with each purpose agnostic for cancer type). MSAC noted that the Project has deviated from that aim. However, MSAC noted that there are currently people who need this technology (which has accepted utility and safety), and yet a full MSAC assessment process is expected to assess its value in cost-effectiveness terms. MSAC noted that most of these applications are from the Australasian Association of Nuclear Medicine Specialists (AANMS). The question is, if MSAC agrees that there are patients who are having FDG PET/CT without a rebate from Medicare, how can the value of this be demonstrated without expending the resources required to undertake a full MSAC assessment?

In this context, MSAC noted that using FDG PET/CT for common cancer types would mean that there are greater financial implications because of the greater number of patients. MSAC therefore considered that there were several directions to go to evaluate the currently unfunded uses of FDG PET/CT in FDG-avid cancer types. One way would be to limit the next step to just an evaluation of initial staging in currently unfunded common cancer types, noting the identified caveats of applying a truncated GEM. An alternative would be to limit the next step to purposes subsequent to initial staging in currently unfunded uncommon or rare cancer types, which would incur multiple uses per patient and therefore greater financial implications. Other alternatives could be various combinations of these first two options. All options could be put to potential applicants (likely AANMS) to gauge their preference in making an application, noting that this would most likely be processed as a Department contracted assessment report (DCAR) given its complexity.

MSAC suggested that the next steps are for the Department to consult with AANMS and share the results of using the GEM for initial staging of rare or uncommon cancer types, as well as to determine the next stages of the PET Project.

### **Application No. 1562 – Streamlining of MSAC assessment of positron emission tomography (PET) project**

**Date of MSAC consideration: 29 July 2021**

#### **Project update for MSAC – July 2021**

MSAC noted that the current extent of Medicare Benefits Schedule (MBS) funding for positron emission tomography/computed tomography (PET/CT) use is relatively small compared to the current extent of clinically accepted use. As part of the MBS Review, the Diagnostic Imaging Clinical Committee recommended use of four clinically based, cancer agnostic indications for MBS funding of fluorodeoxyglucose positron (FDG) PET/CT: diagnosis, staging, response assessment, and re-staging for suspected residual or recurrent cancer. The PET Project was initiated in recognition of the limited resources and availability of relevant evidence to conduct conventional health technology assessments to evaluate FDG PET/CT across all cancer types and across all purposes. The initial focus of the Project was initial staging of rare or uncommon cancer types, which collectively account for 30% of new cancer diagnoses, and for which an initial set of five eligibility criteria were established to triage the cancer types to be assessed.

MSAC noted that the June 2021 ESC meeting reviewed the Overarching Report for the PET Project and was supportive of the piloting of the generic economic model (GEM) approach for the assessment of rare or uncommon cancer types based on two validation studies and five case studies.

MSAC noted that it been requested to:

- support/reject/defer MBS funding for the rare or uncommon cancer types assessed to date
- make recommendations regarding publication of the Project report
- make recommendations regarding the assessments to be conducted in the next phase of this Project.

MSAC noted the overarching aims of the PET Project:

- explore the feasibility of facilitated assessments of FDG PET/CT in rare or uncommon cancer types for diagnosis, initial staging, re-staging for suspected residual or recurrent disease, treatment response assessment and monitoring

- explore the feasibility of facilitated assessments of FDG PET/CT for the purposes as above, but in common cancer types
- explore the feasibility of facilitated assessments of FDG PET/CT outside oncology, and for assessments of other imaging modalities.

MSAC noted that to date, the specific aims were to explore the development of a streamlined approach to assessing FDG PET/CT for initial staging to detect metastatic disease in rare or uncommon cancer types. MSAC acknowledged that the progress of the Project was well regarded by those providers of FDG PET/CT who have been involved in the Project.

MSAC noted that, for the purpose of initial staging, the GEM used a truncated time horizon (12 months) because of modelling complexities and the intention to later add downstream FDG PET/CT purposes with an extended time horizon. This decision reduced the complexity of the model by excluding subsequent interventions (both subsequent investigations and subsequent treatments) beyond those initially informed by the initial staging scan. It also reduced the number of additional inputs to inform the model. However, it also reduced the capacity of the model to fully capture net health gains attributable to the initial change in treatment options. One consequence of this truncation decision is that the utility gains in a CUA may be underestimated by the GEM, especially for those cancer types with a good prognosis beyond 12 months when the patient receives the correct treatment. However, this means that the GEM's cost-effectiveness (incremental cost per extra improved treatment allocation decision) and truncated cost-utility (ICER/QALY) results are difficult to interpret, and it highlights the need to understand the drivers of the GEM through examination of these results across its seven applications. This is particularly the case when the corrected change in treatment is to recommend more intense treatment, because the associated disutility and increased costs are captured in the first 12 months, but health gains beyond 12 months are omitted.

MSAC noted that the validation exercises in breast cancer and prostate cancer supported acceptance of the GEM as they generated results in the same quadrant of the cost-effectiveness plane (increased costs and improved health outcomes). More convincing quantitative validation was impeded by the decision to truncate the GEM for initial staging purposes to a 12-month time horizon. MSAC recognised the value in extending the time horizon but noted that it would not be a simple matter as it would require the addition of Markov or other modelling.

MSAC therefore accepted ESC's advice that the incremental cost per extra improved treatment allocation decision should be interpreted alongside the 12-month ICER/QALY for each cancer type.

MSAC reviewed the table comparing these GEM results for the two validation cancer types and the five case studies, as suggested by ESC. MSAC identified at least two likely drivers of the model: life expectancy without improved treatment, and life expectancy gained with improved treatment. Another driver may be the difference in costs per patient between the treatments for early and metastatic disease.

MSAC agreed with ESC that expert knowledge elicitation is a resource-intensive process, in terms of preparing the questions to elicit the necessary information in each case, selecting the experts and getting them to effectively communicate with each other, and reaching a consensus across the experts. MSAC considered that, while this method was useful to inform the reported case studies it is not feasible for every rare or uncommon cancer, and that a more facilitated approach will be needed in the future.

MSAC noted that its usual approach is to identify if sufficient evidence is available to demonstrate that an intervention (FDG PET/CT) justifies public funding. The Committee considered the ESC suggestion of an alternative approach which would be for MSAC to accept that FDG PET/CT is a superior imaging modality for detecting metastases in FDG-avid cancers, and thus reverse the burden of proof so that funding is supported unless pre-defined eligibility

criteria are not met. MSAC considered that this approach might be easier to apply for rare or uncommon cancer types, for which the financial cost to the MBS would be small, but harder to apply for common cancer types, for which the financial cost to the MBS would be noticeably greater. In this deliberative context, the relative influence of the “value of knowing” may also need to be considered.

MSAC noted that this Project had been in progress for 3 years so far and acknowledged the concern that many years or even decades could be spent trying to apply a model across every imaging purpose and cancer. MSAC accepted that the GEM provides a pragmatic way forward for further exploration to identify eligibility criteria or rules for assessing funding for initial staging in rare or uncommon cancer types (via facilitated or qualitative assessment), for use in supporting initial staging for common cancer types (via exemplar or quantitative assessment), and potentially for further extension to assess the downstream imaging purposes.

MSAC considered that the optimal time point at which to perform initial staging after initial diagnosis had not been considered in the case studies. For example, MSAC indicated that most anal cancers were cured following initial radiotherapy, suggesting that the likely best time to use FDG PET/CT to detect metastases would be after, not before, the initial therapy. One option to address this might be to consult with those who request initial staging. Another option might be to clearly limit initial staging to once per cancer diagnosis so that the requester of the service is incentivised to determine when best to request it.

MSAC considered that the work to date in the PET Project plausibly suggests that, with the exception of gastro-intestinal stromal tumours (GIST), initial staging with FDG PET/CT could be supported in all the other new cancer types assessed (pancreatic, anal, biliary, Merkel cell and Langerhans cell histiocytosis). MSAC accepted that GIST may not have met the initial triage criteria because it is staged differently, which might support the discriminative ability of the GEM and the criteria. The case of Langerhans cell histiocytosis in particular, was an example of where the early truncation of the model (resulting in a relatively large ICER/QALY estimate) underestimated the expected longer-term health gains of allocation to a more appropriate treatment. However, MSAC had reservations that the underlying drivers of the GEM and their inter-relationships had not been fully elucidated, including with reference to the set of seven truncated cost-utility analyses and cost-effectiveness analyses presented using the GEM. MSAC therefore decided that more clarity is needed so that a facilitated approach based on the proposed expansion to the initial triage eligibility criteria could be defined which, without requiring an extension of the time horizon for the ICER/QALY estimate, could satisfactorily account for the two types of results from the GEM. In this way, it would not take another 3 years to assess six more cancer types.

MSAC noted the need for a clear position and parameters on how to approach this task to enable expansion of this work, firstly to initial staging in other rare or uncommon FDG-avid cancer types, then to initial staging in common FDG-avid cancer types, and then to the wider objectives of the Project.

MSAC decided that the MSAC Executive should have a strategy-setting discussion, to clarify the above principles and request that the PET Working Group be engaged to help prepare for this discussion. The aim for the PET Working Group would be to prepare a paper for the following MSAC Executive meeting so that the matter can be brought back to MSAC for re-consideration in November 2021.

## **Application No. 1562 – Development of an evaluation framework for positron emission tomography (PET) imaging services for cancer**

**Date of MSAC consideration: 28-29 November 2019**

### **Project update for MSAC – November 2019**

MSAC noted the Project aims for Application 1562 – Development of an evaluation framework for positron emission tomography (PET) imaging services for cancer:

- Immediate (Dec 2019 and Jan 2020)
  - Confirm use of the streamlined assessment and generic economic model (GEM) for PET/CT for initial staging of (up to) 10 appropriate cancer types.
- Intermediate (mid-2020)
  - Provide MSAC with a validated, timely and cost-effective approach to assessing PET/CT in fluorine 18 fluorodeoxyglucose (FDG)-avid cancers for the purpose of initial staging.
  - Provide MSAC with evaluation results for nominated cancer types (up to 10).
- Long-term (provisional)
  - Investigate how subsequent use of PET/CT for the purposes of restaging and treatment monitoring should be evaluated using similar methodologies for assessing beyond common cancer types to also assess uncommon or rare cancer types.
  - If the above approach is proven successful, explore the possibility of rolling out the streamlined process and GEM to evaluate other imaging modalities in cancer beyond FDG PET/CT.

An overview of the process can be seen in Figure 1.

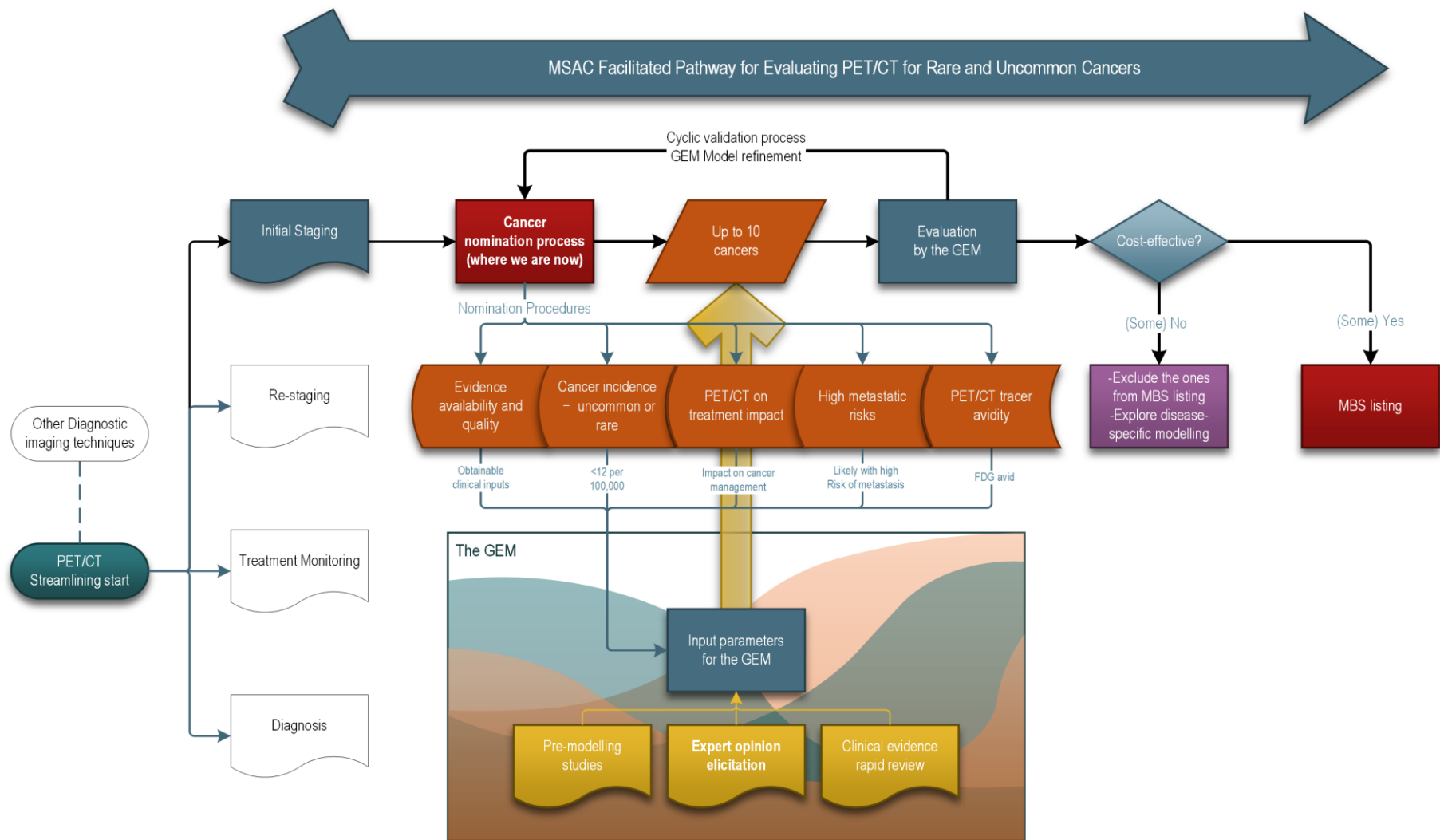


Figure 1: Overview of development process for PET evaluation framework

MSAC noted the outcomes and concerns raised by ESC at its October 2019 meeting. Subsequent responses from the Project team are as follows:

*Why was Markov not used for capturing cost-effectiveness in the long term?* This process is only for initial staging with a focus on immediate benefits: reducing repeated scans, avoiding biopsies and starting of the initial treatment. The benefits are in terms of cost per correct staging using PET.

*How will the model be validated?* Currently it is being tested against the CA1357.1 breast model. There will potentially be testing of the GEM using the lung cancer model. However, MSAC accepted that the use of expert knowledge is inevitable because of the rarity of these conditions. Therefore, the GEM structure requires expert opinion for some model inputs.

*Is this an organ-centric view (per-cancer basis) of malignancy?* The criterion is actually whether it is rapidly dividing and this will be detected using FDG PET/CT. It was clarified that while the PET Working Group refers to 'breast cancer', in fact it is one type of breast cancer that the model is being tested against, and in total ten different types of cancer will be tested. Eligibility criteria into each of the organ-based cancer types would be based on multiple differentiating criteria (including pathology findings), particularly to help differentiate indolent versus aggressive cancer sub-types based on pathology findings. Each one can be considered to be a pilot case and then groupings can be explored.

The concept of a meta-analysis was presented as an analogy of how the combining of individual cancer types could be tested in the model. In the same way that in a meta-analysis results from different studies are combined to produce a summary measure, this Project is exploring the potential of combining different uncommon or rare cancer types (the input parameters). A meta-analysis also produces a measure of heterogeneity to quantify how different the studies are; similarly this Project is planning to explore the differences across uncommon or rare cancer types using sensitivity analyses. In meta-analyses, prediction intervals can be generated to infer the likely result of a "new" or "additional study". The GEM could also produce an overarching probability of a "new" or "additional" cancer being acceptably cost-effective, with some uncertainty measures regarding how likely the incremental cost-effectiveness would remain acceptable. Most importantly, the concept of "combining similar studies" in a meta-analysis will also be borrowed to assess whether it is sensible to group different uncommon or rare cancer types using one single model (i.e. the GEM), as well as producing one summary statistic (e.g. one ICER) as per Table 1.

Table 1: GEM theoretical framework

	<b>STEP 1 – INDIVIDUAL</b>	<b>STEP 2 – GROUPED</b>	<b>STEP 3 – AGGREGATED</b>
<b>Inputs</b>	10 cancer-specific datasets	10 cancer-specific datasets	10 cancer-specific datasets
<b>Data elicitation and validation</b>	Required, confirmed by experts	Required, confirmed by experts	Required, confirmed by experts
<b>Process streamlining</b>	<b>Not grouped</b> , 10 sets of inputs	<b><u>Some</u> grouped</b> , <10 sets of inputs	<b><u>All</u> grouped</b> , only 1 set of inputs
<b>Economic evaluation</b>	10 runs of the generic model	<10 runs of the generic model	1 run of the generic model
<b>Preliminary outcome</b>	10 ICERs	<10 ICERs	1 ICER
<b>Final outcome</b>	(Weighted) averaged ICER	(Weighted) averaged ICER	–



*Is there too much reliance on experts?* MSAC accepted that a large proportion of input parameters are unlikely to be available from the literature, due to cancer rarity and parameters specifically defined by the GEM structure. There is also a lack of better alternatives, i.e. conventional health technology assessment processes. MSAC noted that the Project proposes to use systematic and methodologically robust approaches to mitigate the risk of any subjective bias.

MSAC agreed with the Project team that ideally the ten nominated cancer types will cover a broad range, to test the model more thoroughly. There will be a call for nominations. MSAC was advised that the model needs to be considered from multiple perspectives, including pathologists and those treating childhood cancer, so the nomination form needs to be sent to a range of types of health professionals.

MSAC queried whether there will be confusion between the terminology of M1 and M1+ and would it be better to have M1 and M2 instead? It was clarified that the plus (+) signals that it is advanced. It was thought to be important to separate cases with oligometastatic disease from other more disseminated disease. MSAC considered that the PET Working Group should ensure this is made clear.

MSAC noted that Department representatives will be going to a course in Sheffield (UK), run by world leaders in expert elicitation processes. The intention is to try and develop a robust method for eliciting expert input without bias that can be incorporated into MSAC processes and potentially published.

MSAC noted the Project update and supported the future plans.

MSAC noted that the Department will determine whether the Project can proceed further after the July 2020 MSAC meeting has reviewed the model results for the purpose of initial staging.

MSAC noted that consumer input will be needed at a later stage.