BlueCross BlueShield Federal Employee Program.

FEP Medical Policy Manual

FEP 6.01.26 Oncologic Applications of Positron Emission Tomography Scanning

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Related Policies:

5.21.191 Pluvicto
6.01.06 - Miscellaneous (Noncardiac, Nononcologic) Applications of Fluorine 18 Fluorodeoxyglucose Positron Emission Tomography
6.01.20 - Cardiac Applications of Positron Emission Tomography Scanning
6.01.51 - Interim Positron Emission Tomography Scanning in Oncology to Detect Early Response During Treatment

Oncologic Applications of Positron Emission Tomography Scanning

Description

Positron emission tomography (PET) scans are based on the use of positron-emitting radionuclide tracers coupled to organic molecules, such as glucose, ammonia, or water. The radionuclide tracers simultaneously emit 2 high-energy photons in opposite directions that can be simultaneously detected (referred to as coincidence detection) by a PET scanner, comprising multiple stationary detectors that encircle the area of interest.

A variety of tracers are used for positron emission tomography (PET) scanning, including oxygen 15, nitrogen 13, carbon 11 choline, fluorine 18, gallium 68, fluciclovine 18, and copper 64. Because of their short half-life, some tracers must be made locally using an onsite cyclotron. The radiotracer most commonly used in oncology imaging has been fluorine 18 coupled with fluorodeoxyglucose (FDG), which correlates with glucose metabolism. Fluorodeoxyglucose has been considered useful in cancer imaging because tumor cells show increased metabolism of glucose. The most common malignancies studied have been melanoma, lymphoma, lung, colorectal, and pancreatic cancer.

This evidence review focuses on the use of radiotracers detected with dedicated PET scanners. Radiotracers, such as FDG, may be detected using single-photon emission computerized tomography cameras, a technique that may be referred to as FDG-single-photon emission computerized tomography imaging. The use of single-photon emission computerized tomography cameras for PET radiotracers presents unique issues of diagnostic performance and is not considered herein.

OBJECTIVE

The objective of this evidence review is to examine whether the use of positron emission tomography for the diagnosis, staging and restaging, and/or surveillance of various carcinomas improves the net health outcome in individuals with cancer.

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POLICY STATEMENT

All policy statements apply to both positron emission tomography (PET) scans and PET plus computed tomography (CT) scans (i.e., PET scans with or without PET/CT fusion).

For the clinical situations indicated that may be considered medically necessary, this assumes that the results of the PET scan will influence treatment decisions. If the results will not influence treatment decisions, these situations would be considered not medically necessary.

Bladder Cancer

PET scanning may be considered **medically necessary** in the staging or restaging of muscle-invasive bladder cancer when CT or magnetic resonance imaging are not indicated or remained inconclusive on distant metastasis.

PET scanning is considered **investigational** for bladder tumors that have not invaded the muscle (stage less than cT2).

Bone Sarcoma

PET scanning may be considered **medically necessary** in the staging or restaging of Ewing sarcoma and osteosarcoma.

PET scanning is considered **investigational** in the staging of chondrosarcoma.

Brain Cancer

PET scanning may be considered **medically necessary** in the staging or restaging of brain cancer.

Breast Cancer

PET scanning may be considered **medically necessary** in the staging or restaging of breast cancer for the following application:

- Detecting locoregional or distant recurrence or metastasis (except axillary lymph nodes) when suspicion of disease is high and other imaging is inconclusive.

PET scanning is considered **investigational** in the evaluation of breast cancer for all other applications, including but not limited to the following:

- Differential diagnosis in patients with suspicious breast lesions or an indeterminate or low suspicion finding on mammography
- Staging axillary lymph nodes.
- Predicting pathologic response to neoadjuvant therapy for locally advanced disease.

Cervical Cancer

PET scanning may be considered **medically necessary** in the initial staging of patients with locally advanced cervical cancer.

PET scanning may be considered **medically necessary** in the evaluation of known or suspected recurrence.

Colorectal Cancer

PET scanning may be considered **medically necessary** as a technique for

- Staging or restaging to detect and assess resectability of hepatic or extrahepatic metastases of colorectal cancer, and
- To evaluate a rising and persistently elevated carcinoembryonic antigen levels when standard imaging, including CT scan, is negative.

PET scanning is considered **investigational** as:

- A technique to assess the presence of scarring versus local bowel recurrence in patients with previously resected colorectal cancer.
- A technique contributing to radiotherapy treatment planning.

Endometrial Cancer

PET scanning is considered **medically necessary** in the:

- Detection of lymph node metastases, and
- Assessment of endometrial cancer recurrence.

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Esophageal Cancer

PET scanning may be considered **medically necessary** in the

- Staging of esophageal cancer, and
- Determining response to preoperative induction therapy.

PET scanning is considered **investigational** in other aspects of the evaluation of esophageal cancer, including but not limited to the following applications:

- Detection of primary esophageal cancer.

Gastric Cancer

PET scanning may be considered **medically necessary** in the:

- Initial diagnosis and staging of gastric cancer, and
- Evaluation for recurrent gastric cancer after surgical resection, when other imaging modalities are inconclusive.

Head and Neck Cancer

PET scanning may be considered **medically necessary** in the evaluation of head and neck cancer in the

- Initial diagnosis of suspected cancer,
- Initial staging of disease, and restaging of residual or recurrent disease during follow-up, and
- Evaluation of response to treatment.

Lung Cancer

PET scanning may be considered **medically necessary** for any of the following applications:

- Patients with a solitary pulmonary nodule as a single scan technique (not dual-time) to distinguish between benign and malignant disease when prior CT scan and chest x-ray findings are inconclusive or discordant,
- As staging or restaging technique in those with known non-small-cell lung cancer, and
- To determine resectability for patients with a presumed solitary metastatic lesion from lung cancer.

PET scanning may be considered **medically necessary** in staging of small-cell lung cancer if limited stage is suspected based on standard imaging.

PET scanning is considered **investigational** in staging of small-cell lung cancer if extensive stage is established and in all other aspects of managing small-cell lung cancer.

Lymphoma, Including Hodgkin Disease

PET scanning may be considered **medically necessary** as a technique for staging lymphoma either during initial staging or for restaging at follow-up.

Melanoma

PET scanning may be considered **medically necessary** as a technique for assessing extranodal spread of malignant melanoma at initial staging or at restaging during follow-up treatment for advanced disease (stage III or IV).

PET scanning is considered **investigational** in managing stage 0, I, or II melanoma.

PET scanning is considered **investigational** as a technique to detect regional lymph node metastases in patients with clinically localized melanoma who are candidates to undergo sentinel node biopsy.

Multiple Myeloma

PET scanning may be considered **medically necessary** in the staging or restaging of multiple myeloma, particularly if the skeletal survey is negative.

Neuroendocrine Tumors

PET scanning with gallium 68 and copper 64 may be considered **medically necessary** as a technique for staging neuroendocrine tumors either during initial staging or for restaging at follow-up.

PET scanning with other radiotracers is considered **investigational** in all aspects of managing neuroendocrine tumors.

Ovarian Cancer

PET scanning may be considered **medically necessary** in the evaluation of patients with signs and/or symptoms of suspected ovarian cancer recurrence (restaging) when standard imaging, including CT scan, is inconclusive.

PET scanning is considered **investigational** in the initial evaluation of known or suspected ovarian cancer in all situations.

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Pancreatic Cancer

PET scanning may be considered **medically necessary** in the initial diagnosis and staging of pancreatic cancer when other imaging and biopsy are inconclusive.

PET scanning is considered **investigational** as a technique to evaluate other aspects of pancreatic cancer.

Penile Cancer

PET scanning may be considered **medically necessary** for staging and restaging in patients with suspected inguinal lymph node positive disease.

PET scanning is considered **investigational** in all other aspects of managing penile cancer.

Prostate Cancer

PET scanning with carbon 11 choline and fluorine 18 fluciclovine may be **medically necessary** for evaluating suspected or biochemically recurrent prostate cancer after primary treatment to detect small volume disease in soft tissues.

PET scanning with gallium 68-prostate-specific membrane antigen (i.e., Locametz) or another FDA approved PSMA-11 imaging agent specifically to select mCRPC patients for use of a targeted radioligand therapeutic agent (Pluvicto) is **medically necessary.**

PET scanning for all other indications in known or suspected prostate cancer is considered **investigational.**

Renal Cell Carcinoma

PET scanning is considered **investigational** in all aspects of managing renal cancer.

Soft Tissue Sarcoma

PET scanning is considered **investigational** in evaluation of soft tissue sarcoma, including but not limited to the following applications:

- Distinguishing between benign lesions and malignant soft tissue sarcoma,
- Distinguishing between low-grade and high-grade soft tissue sarcoma,
- Detecting locoregional recurrence, and
- Detecting distant metastasis.

PET scanning is considered **medically necessary** for evaluating response to imatinib and other treatments for gastrointestinal stromal tumors.

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Testicular Cancer

PET scanning may be considered **medically necessary** in evaluation of residual mass following chemotherapy of stage IIB and III seminomas (the scan should be completed no sooner than 6 weeks after chemotherapy).

Except as noted above for seminoma, PET scanning is considered **investigational** in evaluation of testicular cancer, including but not limited to the following applications:

- Initial staging of testicular cancer,
- Distinguishing between viable tumor and necrosis/fibrosis after treatment of testicular cancer, and
- Detection of recurrent disease after treatment of testicular cancer.

Thyroid Cancer

PET scanning may be considered **medically necessary** in the restaging of patients with differentiated thyroid cancer when thyroglobulin levels are elevated and whole-body iodine-131 imaging is negative.

PET scanning is considered **investigational** in the evaluation of known or suspected differentiated or poorly differentiated thyroid cancer in all other situations.

Cancer of Unknown Primary

PET scanning may be considered **medically necessary** in patients with a cancer of unknown primary who meet ALL of the following criteria:

- In patients with a single site of disease outside the cervical lymph nodes, and
- Patient is considering local or regional treatment for a single site of metastatic disease, and
- After a negative workup for an occult primary tumor, and
- PET scan will be used to rule out or detect additional sites of disease that would eliminate the rationale for local or regional treatment.

PET scanning is considered **investigational** for other indications in patients with a cancer of unknown primary, including, but not limited to the following:

- As part of the initial workup of a cancer of unknown primary, and
- As part of the workup of patients with multiple sites of disease.

Cancer Surveillance

PET scanning is considered **investigational** when used as a surveillance tool for patients with cancer or with a history of cancer. A scan is considered surveillance if performed more than 6 months after completion of cancer therapy (12 months for lymphoma) in patients without objective signs or symptoms suggestive of cancer recurrence (see Policy Guidelines section).

POLICY GUIDELINES

Patient Selection

As with any imaging technique, the medical necessity of positron emission tomography (PET) scanning depends in part on what imaging techniques are used before or after the PET scanning. Due to its expense, PET scanning is typically considered after other techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), or ultrasonography, provide inconclusive or discordant results. In patients with melanoma or lymphoma, PET scanning may be considered an initial imaging technique. If so, the medical necessity of subsequent imaging during the same diagnostic evaluation is unclear. Thus, PET should be considered for the medically necessary indications above only when standard imaging (eg, CT, MRI) is inconclusive or not indicated.

Patient selection criteria for PET scanning may also be complex. For example, it may be difficult to determine from claims data whether a PET scan in a patient with malignant melanoma is being done primarily to evaluate extranodal disease or regional lymph nodes. Similarly, it may be difficult to determine whether a PET scan in a patient with colorectal cancer is being performed to detect hepatic disease or evaluate local recurrence. Due to the complicated hierarchy of imaging options in patients with malignancy and complex patient selection criteria, a possible implementation strategy for this policy is its use for retrospective review, possibly focusing on cases with multiple imaging tests, including PET scans.

Use of PET scanning for surveillance as described in the policy statement and policy rationale refers to the use of PET to detect disease in asymptomatic patients at various intervals. This is not the same as the use of PET for detecting recurrent disease in symptomatic patients; these applications of PET are considered within tumor-specific categories in the policy statements.

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Coding

A PET scan involves 3 separate activities: (1) manufacture of the radiopharmaceutical, which may be on site or at a regional center with delivery to the institution performing PET; (2) actual performance of the PET scanner; and (3) interpretation of the results. There are Current Procedural Terminology (CPT) and Healthcare Common Procedure Coding System (HCPCS) codes available to code for PET scans.

When the radiopharmaceutical is provided by an outside distribution center, there may be an additional separate charge, or this charge may be passed through and included in the hospital bill. In addition, an extra transportation charge will be likely for radiopharmaceuticals that are not manufactured on site.

The Centers for Medicare & Medicaid Services added 2 new modifiers in 2009 to facilitate the changes in the Medicare national coverage policy for PET. The modifiers are:

> PI - Positron emission tomography (PET) or PET/computed tomography (CT) to inform the initial treatment strategy of tumors that are biopsy proven or strongly suspected of being cancerous based on other diagnostic testing, 1 per cancer diagnosis.
>
> PS - Positron emission tomography (PET) or PET/computed tomography (CT) to inform the subsequent treatment strategy of cancerous tumors when the beneficiary's treating physician determines that the PET study is needed to inform subsequent anti-tumor strategy.

BENEFIT APPLICATION

Experimental or investigational procedures, treatments, drugs, or devices are not covered (See General Exclusion Section of brochure).

FDA REGULATORY STATUS

The U.S. Food and Drug Administration (FDA) website includes various PET-related documents.[1]

As of August 2021 , the following radiopharmaceuticals have been granted approval by the FDA, to be used with PET for carcinoma-related indications (see Table 1).[2]

Table 1. Radiopharmaceuticals Approved for Use With PET for Oncologic Applications

Radiopharmaceutical	Manufacturer	Name	Carcinoma-Related Indication With PET
Carbon-11 choline (C-11)	Various		Suspected prostate cancer recurrence based on elevated blood PSA after therapy and noninformative bone scintigraphy, CT, or MRI
Copper-64 dotatate	Curium	Detectnet™	Localization of somatostatin receptor-positive NETs in adult patients
Fluorine-18 fluorodeoxyglucose (FDG)	Various		Suspected or existing diagnosis of cancer, all types
Fluorine-18 fluoroestradiol	Zionexa USA	Cerianna™	Detection of ER-positive lesions as an adjunct to biopsy in patients with recurrent or metastatic breast cancer
Fluorine-18 fluciclovine	Blue Earth Diagnostics	Axumin™	Suspected prostate cancer recurrence based on elevated blood PSA levels after treatment
Gallium-68 dotatoc	UIHC - P E T Imaging Center		Localization of somatostatin receptor-positive NETs in adult and pediatric patients
Gallium-68 dotatate	Advanced Accelerator Applications	NETSPOT™	Localization of somatostatin receptor-positive NETs in adult and pediatric patients
Gallium-68 PSMA-11	University of California, Los Angeles and the University of California, San Francisco		PSMA positive lesions in men with prostate cancer with suspected metastasis who are candidates for initial definitive therapy or with suspected recurrence based on elevated serum PSA level
Piflufolastat fluorine-18	Progenics Pharmaceuticals, Inc	Pylarify	PSMA positive lesions in men with prostate cancer with suspected metastasis who are candidates for initial definitive therapy or with suspected recurrence based on elevated serum PSA level

FDA-approval given to the University of California, Los Angeles and the University of California, San Francisco.
CT: computerized tomography; ER: estrogen receptor; MRI: magnetic resonance imaging; NET: neuroendocrine tumors; PET: positron emission tomography; PSA: prostate-specific antigen; PSMA: prostate-specific membrane antigen.

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RATIONALE

Summary of Evidence

Bladder Cancer

For individuals who have suspected or diagnosed bladder cancer in need of staging or restaging information who receive ^{18}F coupled with fluorodeoxyglucose positron emission tomography (FDG PET) or fluorodeoxyglucose- positron emission tomography/computed tomography (FDG-PET/CT), the evidence includes a systematic review and meta-analysis. Relevant outcome is test validity. Pooled analyses showed relatively high sensitivity and specificity for muscle-invasive bladder cancer. Clinical guidelines include positron emission tomography (PET) and positron emission tomography/computed tomography(PET/CT) as considerations in staging muscle-invasive bladder cancer, though computed tomography (CT), magnetic resonance imaging, and chest radiographs are also appropriate techniques for staging purposes. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing bladder cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Bone Sarcoma

For individuals who have suspected or diagnosed bone sarcoma and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes systematic reviews and meta-analyses. Relevant outcome is test validity. Pooled analyses have shown that PET or PET/CT can effectively diagnose and stage bone sarcoma, including chondrosarcoma. Use of PET or PET/CT has high sensitivities and specificities in detecting metastases in bone and lymph nodes; however, the tests have low sensitivity in detecting lung metastases. Clinical guidelines include PET and CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing bone sarcoma treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Brain Tumors

For individuals who have diagnosed brain tumors and in need of staging or restaging information or who have suspected brain tumor who receive FDG-PET, ^{18}F fluoroethyl-l-tyrosine (^{18}F FET-PET), or ^{11}C methionine PET, the evidence includes several systematic reviews and meta-analyses. Relevant outcome is test validity. Pooled analyses have shown that PET or PET/CT can be effective in distinguishing brain tumors from normal tissue. Indirect comparisons between the radiotracers ^{11}C-methionine and FDG have shown that ^{11}C-methionine may have better diagnostic performance. Clinical guidelines include PET to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing brain cancer treatment who receive FDG-PET, ^{18}F FET-PET, or ^{11}C-methionine PET, the evidence includes systematic reviews and meta-analyses. Relevant outcome is test validity. Pooled analyses did not support the use of PET for surveillance of brain cancer following treatment. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Breast Cancer

For individuals who have diagnosed breast cancer and inconclusive results from other imaging techniques who receive adjunctive FDG-PET or FDG-PET/CT for staging or restaging, the evidence includes meta-analyses. Relevant outcome is test validity. While studies included in the meta-analyses reported variability in estimates of sensitivity and specificity, FDG-PET or FDG-PET/CT may be helpful in situations in which standard staging results are equivocal or suspicious, particularly in patients with locally advanced or metastatic disease. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected or diagnosed breast cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment, several systematic reviews, and meta-analyses. Relevant outcome is test validity. There is no evidence supporting the use of PET in diagnosing breast cancer. The false-negative rates (5.5% to 8.5%) using PET in patients with breast cancer can be considered unacceptable, given that breast biopsy can provide more definitive results. Use of PET/CT may be considered for the detection of metastases only when results from other imaging techniques are inconclusive. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing breast cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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Cervical Cancer

For individuals who have diagnosed cervical cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes an Agency for Healthcare Research and Quality (AHRQ) report and meta-analyses. Relevant outcome is test validity. Pooled results have shown that PET can be used for staging or restaging and for detecting recurrent disease. Clinical guidelines include PET and CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected cervical cancer or who are asymptomatic after completing cervical cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcomes are test accuracy and test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Colorectal Cancer

For individuals who have diagnosed colorectal cancer (CRC) and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes several meta-analyses. Relevant outcome is test validity. A meta-analysis evaluating the diagnostic accuracy of PET or PET/CT found a high sensitivity but low specificity. Several pooled analyses evaluating staging or restaging using PET or PET/CT resulted in wide ranges of sensitivities and specificities, from 16% to 99%. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected CRC or who are asymptomatic after completing CRC treatment who receive FDG-PET or FDG-PET/CT, the evidence includes a RCT. Relevant outcome is test validity. The RCT found no differences in outcomes when FDG-PET/CT was added to usual surveillance compared to usual surveillance only. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Endometrial Cancer

For individuals who have diagnosed endometrial cancer in need of staging or restaging information or who are asymptomatic after completing endometrial cancer treatment who receive FDG-PET or FDG-PET/CT, the evidence includes a systematic review and meta-analysis. Relevant outcome is test validity. Pooled estimates from the meta-analysis showed high sensitivities and specificities for FDG-PET/CT in detecting lymph node metastases and endometrial cancer recurrence following treatment. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Esophageal Cancer

For individuals who have diagnosed esophageal cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes several meta-analyses. Relevant outcome is test validity. Pooled estimates have shown high sensitivities and specificities compared to other diagnostic imaging techniques. Clinical guidelines include PET and CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected esophageal cancer or who are asymptomatic after completing esophageal cancer treatment who receive FDG-PET or FDG-PET/CT, the evidence includes meta-analyses. Relevant outcome is test validity. Pooled analyses have shown adequate sensitivities but low specificities. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Gastric Cancer

For individuals who have suspected or diagnosed gastric cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes several meta-analyses. Relevant outcome is test validity. Pooled analyses, with sensitivities and specificities ranging from 78% to 88%, have shown that PET or PET/CT can inform staging or restaging of patients with gastric cancer. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing gastric cancer treatment who receive FDG-PET or FDG-PET/CT, the evidence includes meta-analyses. Relevant outcome is test validity. Pooled analyses have shown low sensitivities and specificities. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Head and Neck Cancer

For individuals who have suspected or diagnosed head and neck cancer in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes several systematic reviews and meta-analyses. Relevant outcome is test validity. In patients with head and neck cancers, PET and PET/CT are better able to detect local and metastatic disease compared with other imaging techniques. Evidence has also shown that FDG-PET/CT may be useful in predicting response to therapy. Two meta-analyses calculated the ability of FDG-PET or PET/CT to detect the residual or recurrent disease during various stages of treatment and another meta-analysis calculated the ability of positive PET or PET/CT results to predict OS and event-free survival. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing head and neck cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Non-Small-Cell Lung Cancer

For individuals who have suspected non-small cell lung cancer (NSCLC) and inconclusive results from other imaging techniques or who have diagnosed NSCLC and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes several meta-analyses. Relevant outcome is test validity. Pooled analyses have shown that PET and PET/CT have better diagnostic performance than conventional imaging techniques. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected NSCLC or who are asymptomatic after completing NSCLC treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Small-Cell Lung Cancer

For individuals with diagnosed small-cell lung cancer (SCLC) and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes systematic reviews and meta-analyses. Relevant outcome is test validity. While the quality of the studies was considered low, PET and PET/CT can be considered for staging or restaging in patients with SCLC if a limited stage is suspected. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

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For individuals who have suspected SCLC or who are asymptomatic after completing SCLC treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcomes are test accuracy and test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Hodgkin and Non-Hodgkin Lymphoma

For individuals who have suspected or diagnosed Hodgkin and non-Hodgkin lymphoma in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment, several meta-analyses, and a random controlled trial (RCT). Relevant outcome is test validity. Both PET and PET/CT have been found to provide useful information in the management of Hodgkin and non-Hodgkin lymphoma. The Deauville 5-point scale was developed based on PET results and can be used for staging and treatment response for patients with lymphoma. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing Hodgkin lymphoma treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing non-Hodgkin lymphoma treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Melanoma

For individuals who have suspected or diagnosed stage I or II melanoma and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment. Relevant outcome is test validity. Evidence has shown PET and PET/CT are not as beneficial as the reference standard (sentinel node biopsy) for assessing regional lymph nodes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have diagnosed advanced melanoma (stage III or IV) and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment and a meta-analysis. Relevant outcome is test validity. Evidence has shown PET and PET/CT can detect systemic metastases in patients with advanced melanoma. Clinical guidelines include PET/CT for staging or restaging stage III or IV disease and for surveillance. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing melanoma treatment who receive FDG-PET or FDG-PET/CT, the evidence includes retrospective and observational studies. Relevant outcome is test validity. At the discretion of the physician, imaging surveillance can be considered every 3 to 12 months. Because recurrences usually occur within 3 years, screening asymptomatic patients beyond 3 to 5 years is not recommended. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

Multiple Myeloma

For individuals who have suspected or diagnosed multiple myeloma in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes systematic reviews and a prospective, comparative study. Relevant outcome is test validity. The meta-analysis reported high sensitivity in detecting extramedullary lesions in patients with multiple myeloma. The sensitivity of FDG-PET was greater than whole body x-ray in a meta-analysis and was similar to whole-body MRI, with MRI having a higher sensitivity for detecting skull and spine bone lesions, in a prospective evaluation. Clinical guidelines include PET/CT on the list of imaging techniques that may be useful for initial workup, as well as follow-up and surveillance as indicated. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing multiple myeloma treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Neuroendocrine Tumors

For individuals who have suspected or diagnosed neuroendocrine tumors and in need of staging or restaging information or who are asymptomatic after completing neuroendocrine tumor treatment who receive FDG-PET or FDG-PET/CT, the evidence includes 2 meta-analyses. Relevant outcome is test validity. The evidence did not compare PET or PET/CT with other modalities and, therefore, did not provide comparative effectiveness information. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected or diagnosed neuroendocrine tumors and in need of staging or restaging information who receive gallium 68 (^{68}Ga) or copper 64 PET or PET/CT (^{64}Cu PET or PET/CT), the evidence includes several systematic reviews with meta-analyses and prospective, comparative studies. Relevant outcome is test validity. The meta-analyses showed relatively high sensitivities and specificities using ^{68}Ga-PET/CT as the radiotracer compared with other imaging techniques in the diagnosis and staging of neuroendocrine tumors. A study comparing the diagnostic performance between ^{64}Cu PET/CT and ^{68}Ga-PET/CT reported an increase in detection of lesions with ^{64}Cu PET/CT. Current guidelines recommend using somatostatin receptor PET tracers, ^{68}Ga-dotatate, ^{68}Ga-dotatoc, or ^{64}Cu-dotatate, to assess receptor status and presence of distant disease. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing neuroendocrine tumor treatment who receive^{68}Ga or ^{64}Cu PET or PET/CT , there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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Ovarian Cancer

For individuals who have diagnosed ovarian cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes an AHRQ systematic review and several meta-analyses. Relevant outcome is test validity. Pooled sensitivities and specificities have supported the use of PET and PET/CT for the detection of recurrent ovarian cancer. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected ovarian cancer or who are asymptomatic after completing ovarian cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Pancreatic Cancer

For individuals who have suspected or diagnosed pancreatic cancer and with inconclusive results from other imaging techniques who receive adjunctive FDG-PET or FDG-PET/CT for staging or restaging, the evidence includes a TEC Assessment, systematic reviews, and a large observational study. Relevant outcome is test validity. The evidence has shown that PET and PET/CT do not have a high enough negative predictive value to surpass current standard decision thresholds. The large observational study, which assessed the incremental diagnostic value of PET/CT when added to standard workup with CT, showed significant improvements in sensitivity and specificity compared with CT alone. Clinical guidelines state that PET or PET/CT should only be considered if the results from standard staging methods are inconclusive. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected or diagnosed pancreatic cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes an AHRQ systematic review, a TEC Assessment, and a meta-analysis published after the review and assessment. Relevant outcome is test validity. The evidence has shown that PET and PET/CT do not have a high enough NPV to surpass current standard decision thresholds. Therefore, PET or PET/CT should only be considered if the results from standard staging methods are inconclusive. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing pancreatic cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Penile Cancer

For individuals who have suspected or diagnosed node negative penile cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a systematic review. Relevant outcome is test validity. The evidence has shown that PET had a low sensitivity, and no comparisons were made with other modalities. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected or diagnosed node positive penile cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a systematic review and a retrospective comparative study. Relevant outcome is test validity. In patients with suspected inguinal lymph node positive disease, PET/CT may offer increased sensitivity compared to CT alone for staging. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing penile cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Prostate Cancer

For individuals who have suspected or diagnosed prostate cancer and in need of staging or restaging information who receive ^{11}C-choline PET, ^{11}C-choline PET/CT, ^{18}F-fluciclovine PET, or ^{18}F-fluciclovine PET/CT, the evidence includes several meta-analyses. Relevant outcome is test validity. Meta-analyses have reported that use of ^{11}C-choline and ^{18}F-fluciclovine radiotracers result in similar sensitivities and specificities. Prospective studies in men with biochemical recurrence after primary treatment have reported that a majority of management decisions were changed based on ^{18}F-fluciclovine PET/CT results among men with suspected recurrence. One of those studies evaluated the impact on clinical outcomes and reported an increase in 3-year event-free survival rates. Further study is needed to compare PET and PET/CT with other imaging techniques, such as MRI and radionuclide bone scan. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing prostate cancer treatment who receive ^{11}C-choline PET, ^{11}C-choline PET/CT, ^{18}F-fluciclovine PET, or^{18}F-fluciclovine PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Prostate-specific membrane antigen (PSMA)-targeted radiotracers are required to detect PSMA- which is a requirement for treatment with Pluvicto.

For individuals who are asymptomatic after completing prostate cancer treatment who receive ^{68}Ga-PSMA PET, ^{68}Ga-PSMA PET/CT, piflufolastat-F^{18} PET, and piflufolastat-F^{18} PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Renal Cell Carcinoma

For individuals who are diagnosed with renal cell carcinoma and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes a systematic review and meta-analysis. Relevant outcome is test validity. The review concluded that PET has the potential to detect metastatic or recurrent lesions in patients with renal cell cancer but that additional prospective studies are needed. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Soft Tissue Sarcoma

For individuals who have diagnosed soft tissue sarcoma and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes an AHRQ review and a systematic review using PET for assessing response to imatinib. Relevant outcome is test validity. The review reported that PET had low diagnostic accuracy and there was a lack of studies comparing PET with alternative diagnostic modalities. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with diagnosed soft tissue sarcoma and in need of rapid reading of response to imatinib treatment who receive FDG-PET or FDG-PET/CT, the evidence includes a systematic review. Relevant outcome is test validity. The review concluded that PET/CT can be used to monitor treatment response to imatinib, which can lead to individually adapted treatment strategies. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected soft tissue sarcoma or who are asymptomatic after completing soft tissue sarcoma treatment who receive FDG-PET or FDG-PET/CT, the evidence includes a systematic review. Relevant outcome is test validity. The review concluded that there was insufficient evidence on the use of PET for the detection of locoregional recurrence. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

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Testicular Cancer

For individuals with diagnosed testicular cancer in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes an AHRQ systematic review and assessment. Relevant outcome is test validity. Results have shown that PET or PET/CT can evaluate residual masses following chemotherapy for seminoma. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. There is no evidence supporting the use of PET or PET/CT in nonseminoma patients. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected testicular cancer or who are asymptomatic after completing testicular cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Thyroid Cancer

For individuals with diagnosed thyroid cancer and in need of staging or restaging information who receive FDG-PET or FDG-PET/CT, the evidence includes systematic reviews and meta-analyses. Relevant outcome is test validity. Pooled analyses have shown that PET or PET/CT can effectively detect recurrent differentiated thyroid cancer. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have suspected thyroid cancer or who are asymptomatic after completing thyroid cancer treatment who receive FDG-PET or FDG-PET/CT, there is no evidence. Relevant outcome is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Cancer of Unknown Primary and Single-Site Metastatic Disease

For individuals with cancer of unknown primary and single-site metastatic disease who receive FDG-PET or FDG-PET/CT, the evidence includes a TEC Assessment. Relevant outcome is test validity. Studies reviewed in the assessment showed that PET identified previously undetected metastases confirmed by biopsy. Additionally, PET can contribute to the management of patients with cancer of unknown primary. Clinical guidelines include PET/CT to inform management decisions that may offer clinical benefit. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

Bladder Cancer

American College of Radiology

In 2018, the American College of Radiology (ACR) issued an Appropriateness Criteria for pretreatment staging of muscle-invasive bladder cancer.[4,] The ACR stated that FDG-PET/CT "may be appropriate" for the pretreatment staging of muscle-invasive bladder cancer. However, the ACR cited CT, MRI, and chest radiographs as the most appropriate imaging techniques for pretreatment staging.

In 2021 , the ACR issued an Appropriateness Criteria for post-treatment surveillance of bladder cancer. For muscle-invasive bladder cancer, FDG-PET/CT may be appropriate for surveillance; however, the ACR states that chest radiograph, CT, and MRI are usually appropriate procedures.[5,]

National Comprehensive Cancer Network

Current National Comprehensive Cancer Network (NCCN) guidelines for bladder cancer (v.4.2021) state that FDG-PET/CT may be useful in assessing the presence of regional or distant metastases, though it is not the preferred imaging modality.[6,] Recommendations for FDG-PET/CT in muscle-invasive bladder cancer include (all category 2B):

- For chest imaging:
  - Staging: "may be beneficial in selected patients with T2 (muscle-invasive disease) and in patients with ≥cT3 disease"
  - Follow-up with or without cystectomy: "may be performed if not previously done or if metastasis is suspected in selected patients"
  - Follow-up of cT4b and metastatic disease: "may be performed if not previously done or in high-risk patients in whom metastatic disease is suspected"
- For abdominal and pelvic imaging:
  - Staging: "may be useful in selected patients with ≥cT2 disease and may change management in patients with ≥cT3 disease"
  - Follow-up: "may be performed if not previously done or in high-risk patients in whom metastatic disease is suspected; this could also be used to guide biopsy in certain patients"
- Evaluation of suspected bone metastases
  - "Symptomatic, or high-risk patients, or those with laboratory indicators of bone metastasis may be imaged with MRI, FDG-PET/CT (category 2B), or bone scan. FDG-PET/CT (category 2B) may also be considered in cases when additional sites of extraosseous metastatic disease are suspected or previously documented."

However, the guidelines note that "PET/CT should not be used to delineate the anatomy of the upper urinary tract" or in patients with nonmuscle invasive bladder cancer.

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Bone Sarcoma

Current NCCN guidelines for bone cancer (v.1.2022) state that PET/CT may be considered for[11]:

- Diagnostic workup of patients with suspected primary bone cancer, including chordoma, Ewing sarcoma, or osteosarcoma,
- Restaging in patients with Ewing sarcoma or osteosarcoma, and
- Surveillance of patients with Ewing sarcoma or osteosarcoma (category 2B).

Brain Tumors

Current NCCN guidelines for brain cancer (v.1.2021) include these statements:[16]

- PET can assess metabolism within the tumor and normal tissue by using radio-labeled tracers, which may be useful in differentiating tumor from radiation necrosis, may correlate with tumor grade, or provide an optimal area for biopsy.
- Limitations include the accuracy of interpretations and availability of equipment and isotopes.
- Close follow-up imaging, MR perfusion, MR spectroscopy, PET/CT imaging, and repeat surgery may be necessary if clinically indicated. Educate patients on the uncertainty of imaging as a whole, and the potential need for corollary testing to interpret scans.

Breast Cancer

American College of Radiology

In 2017, the ACR issued an Appropriateness Criteria for the initial workup and surveillance for local recurrence and distant metastases in asymptomatic women with stage I breast cancer.[32] The ACR noted that FDG-PET/CT is usually not appropriate during initial workup or surveillance of these patients to rule out metastases.

National Comprehensive Cancer Network

Current NCCN guidelines on breast cancer (v.5.2021) include a category 2B recommendation for FDG-PET/CT as an optional test in the workup of breast cancer.[33]The use of FDG-PET/CT is "most helpful in situations where standard staging studies are equivocal or suspicious. FDG-PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases when used in addition to standard staging studies."

The NCCN recommends against FDG-PET/CT for lower stage breast cancer (I, II, or operable III) due to high false-negative rates in detecting low-grade lesions or lesions less than 1 cm, low sensitivity in detecting axillary node metastasis, the low prior probability of detectable metastases in these patients, and high false-positive rates.

The NCCN guidelines do not recommend routine use of PET in asymptomatic patients for surveillance and follow-up after breast cancer treatment. When monitoring the metastatic disease, the guidelines note that PET is "challenging because of the absence of a reproducible, validated, and widely accepted set of standards for disease activity assessment."

Cervical Cancer

Current NCCN guidelines on cervical cancer (v.1.2021) state that PET/CT may be considered under the following conditions:[38]

- Part of the initial non-fertility and fertility-sparing workup for patients with stage I cervical cancer.
- Part of the initial staging workup for detection of stage II, III, or IV metastatic disease.
- Follow-up/surveillance for stage I (only nonfertility sparing) through stage IV at 3 to 6 months after completion of therapy or if there is suspected recurrence or metastases.
- PET/CT should cover neck, chest, abdomen, pelvis, and groin.

Colorectal Cancer

American College of Radiology

In 2017, the ACR issued Appropriateness Criteria for the pretreatment staging of CRC.[53] In the evaluation of distant metastases, the criteria stated that "routine use of PET/CT is likely not indicated; however, it may provide guidance in cases of advanced, bilobar liver disease to exclude extrahepatic metastases prior to surgical intent to cure."

National Comprehensive Cancer Network

Current NCCN guidelines for colon cancer (v.2.2021) "strongly discourages the routine use of PET/CT scanning for staging, baseline imaging, or routine follow-up" for metastatic disease and "recommend consideration of a preoperative PET/CT scan at baseline only if prior anatomic imaging indicates the presence of potentially surgically curable M1 disease."[54] For initial workup of nonmetastatic patients, the guidelines state that PET/CT is not routinely indicated, and "PET/CT does not supplant a contrast-enhanced diagnostic CT or MR scan and should only be used to evaluate an equivocal finding on a contrast-enhanced CT scan or MR scan or in patients with strong contraindications to IV [intravenous] contrast." PET/CT can be considered in select patients "considered for image-guided liver-directed therapies" and "for assessment of response and liver recurrence after image-guided liver-directed therapies."Otherwise, use of PET/CT is not recommended for surveillance. The NCCN has noted that PET/CT should not be used to assess response to chemotherapy. The NCCN was divided on the appropriateness of PET/CT when carcinoembryonic antigen level is rising; PET/CT might be considered when imaging study results (eg, a good quality CT scan) are normal.

Current NCCN guidelines for rectal cancer (v.1.2021) state that PET/CT is "not routinely indicated" and "should only be used to evaluate an equivocal finding on a contrast-enhanced CT or MR scan or in patients with strong contraindications to IV contrast."[55] For certain patients with potential surgically-curable M1 disease or who are being considered for image-guided liver-directed

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therapies, a PET/CT may be considered. Use of PET/CT is not recommended for restaging or for surveillance with the exception of surveillance in patients who are considered for image-guided liver-directed therapies for hepatic metastases. Use of PET/CT can be considered if serial carcinoembryonic antigen elevation occurs.

Endometrial Cancer

Current NCCN guidelines for endometrial cancer (v.3.2021) state that neck/chest/abdomen/pelvis/groin PET/CT can be considered in the initial workup, in both non-fertility- and fertility-sparing management, if metastases are suspected in select patients (based on clinical symptoms, physical findings, or abnormal laboratory findings).[11,] Whole-body PET/CT may also be considered for patients with suspected recurrence or metastases as clinically indicated. Following treatment, PET/CT can be considered in select patients for surveillance, if findings on MRI or CT imaging require clarification or if metastasis is suspected.

Esophageal Cancer

For initial diagnosis, PET is generally not considered for detecting primary esophageal tumors, and evidence is lacking in its ability to differentiate between esophageal cancer and benign conditions.

Current NCCN guidelines for esophageal cancer (v.4.2021) indicate that PET/CT can be considered under the following conditions:[62,]

- Part of the initial workup if there is no evidence of M1 disease.
- To assess response to preoperative or definitive chemoradiation.
- For staging purposes, prior to surgery to obtain nodal distribution information

The guidelines note that PET/CT for these indications is preferable to PET alone.

Gastric Cancer

Current NCCN guidelines for gastric cancer (v.4.2021) indicate that FDG-PET/CT (but not PET alone) can be used as part of an initial workup if there is no evidence of metastatic disease.[66,] The guidelines note that the accuracy of FDG-PET/CT is lower than for CT alone due to low tracer accumulation in diffuse and mucinous tumor types but specificity for detecting local lymph note involvement is higher. Use of FDG-PET/CT adds value to the diagnostic workup with higher accuracy in staging (identifying tumor and pertinent nodal groups). The NCCN guidelines also indicate that FDG-PET/CT can be used to evaluate response to treatment, in cases of renal insufficiency or allergy to CT contrast. For surveillance in patients with stage II or III disease, FDG-PET/CT can be considered as clinically indicated but CT scan with oral and intravenous contrast is preferred.

Head and Neck Cancer

Current NCCN guidelines on head and neck cancer (v.3.2021) indicate that PET/CT can be appropriate for disease evaluation, for detection of metastases or recurrence, and for evaluation of response to treatment (at a minimum of 12 weeks posttreatment to reduce false-positive rate).[79,] For surveillance of locoregionally advanced disease, an initial 3-month PET/CT scan may be useful, but if the scan is negative, then further routine imaging is not supported in an asymptomatic patient.

Lung Cancer

Non-Small-Cell Lung Cancer

Current NCCN guidelines for NSCLC (v.5.2021) indicate that PET/CT can be used in the staging of the disease, detection of metastases, treatment planning, restaging after adjuvant treatment, and detection of disease recurrence.[90,] The guidelines note that PET is "best performed before a diagnostic biopsy site is chosen in cases of high clinical suspicion for aggressive, advanced-stage tumors." However, PET is not recommended for detection of brain metastasis from lung cancers. While PET/CT is not routinely recommended for surveillance after completion of definitive therapy, it may be considered to differentiate between true malignancies and benign conditions (eg, atelectasis, consolidation, and radiation fibrosis), which may have been detected by CT imaging. If PET/CT detects recurrent disease, biopsy confirmation is necessary prior to initiating additional treatment because FDG remains avid in areas treated with radiation therapy up to 2 years.

Small-Cell Lung Cancer

Current NCCN guidelines for SCLC (v.1.2022) indicate PET/CT can be used in the staging of the disease if limited stage is suspected or if needed to clarify stage. If extensive-stage is established, brain imaging, MRI (preferred), or CT with contrast is recommended. Use of PET/CT "is not recommended for routine follow-up."[94,]

Lymphoma, Including Hodgkin Disease

Current NCCN guidelines for Hodgkin lymphoma (v.4.2021)[105,] and non-Hodgkin lymphomas, including chronic lymphocytic leukemia/small lymphocytic lymphoma [v.4.2021],[106,] B-cell lymphoma [v.2.2020],[107,] primary cutaneous lymphoma [v.2.2021],[108,] and T-cell lymphomas [v.1.2021])[109,] indicate that PET/CT (in some cases PET only) may be used in the diagnostic workup, staging, restaging, and evaluating treatment response. The guidelines recommend using the internationally recognized Deauville 5-point PET scale for initial staging and assessment of treatment response. The following PET/CT results are assigned the corresponding scores: 1=no uptake; 2=uptake ≤ mediastinum; 3=uptake > mediastinum but ≤ liver; 4=uptake moderately higher than liver; and 5=uptake markedly higher than liver and/or new lesions. The Deauville PET scores can be used to determine the course of treatment. The guidelines note that if PET/CT detects 3 or more skeletal lesions, the marrow may be assumed to be involved and marrow biopsies are no longer indicated. The Hodgkin lymphoma guidelines also note "Surveillance PET should not be done routinely due to risks for false-positives. Management decisions should not be based on PET scan alone; clinical or pathologic correlation is needed."[105,]

Melanoma

Current NCCN guidelines for cutaneous melanoma (v.2.2021) indicate that PET/CT can be used at baseline in stage IV disease to evaluate for distant metastases.[112,] For stage III disease, cross-sectional imaging, including PET/CT can be consider at baseline (category 2B) or to assess specific signs and symptoms. Use of PET/CT is not recommended for stage I or II diseases. Also, PET/CT is listed as an option for surveillance screening for recurrence every 3 to 12 months (category 2B) at the physician's discretion. Because most recurrences occur within the first 3

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years, routine screening for asymptomatic recurrence is not recommended beyond 3 to 5 years. The guidelines note that the safety of PET/CT is of concern due to cumulative radiation exposure.

Multiple Myeloma

Current NCCN guidelines for multiple myeloma (v.7.2021) recommend PET/CT as an imaging technique option for initial workup.[117.] The NCCN recommends using PET/CT for follow-up and surveillance as indicated, ideally if utilized for initial workup. Use of PET/CT is considered first choice during initial work up of solitary extraosseous plasmacytoma. Use of PET/CT may also be considered to detect disease progression.

Neuroendocrine Tumors

Current NCCN guidelines for neuroendocrine tumors (v.3.2021) have recommended somatostatin receptor-based imaging with PET/CT or PET/MRI, using somatostatin receptor PET tracers,^{68}Ga-dotatate, ^{68}Ga-dotatoc, or ^{64}Cu-dotatate,to assess receptor status and presence of distant disease.[124.]Somatostatin receptor imaging can assist in determining if a patient would benefit from receiving a somatostatin receptor-directed therapy. Use of FDG-PET may be considered to identify high-grade active disease in selected patients when high-grade neuroendocrine tumors or poorly differentiated carcinomas are documented or suspected or when disease is growing rapidly. For certain types of neuroendocrine tumors (eg, well-differentiated, grade 3), somatostatin receptor-based imaging with PET/CT or PET/MRI or FDG-PET/CT scans for surveillance are recommended as clinically indicated. Use of ^{18}F-DOPA PET/CT is not discussed in the guidelines.

Ovarian Cancer

American College of Radiology

In 2018, the ACR published Appropriateness Criteria on staging and follow-up of ovarian cancer stating that PET/CT and MRI may be appropriate when lesions are indeterminate with contrast-enhanced CT.[128.]

National Comprehensive Cancer Network

Current NCCN guidelines for ovarian cancer (v.1.2021) indicate that PET/CT can be appropriate "for indeterminate lesions if results will alter management."[129.] Use of PET/CT may be considered for monitoring patients with stage II through IV ovarian cancer receiving adjuvant chemotherapy or after initial treatment (eg, surgery followed by chemotherapy) if clinically indicated. PET/CT also can be considered if clinically indicated after complete remission, for follow-up and for monitoring for recurrence if cancer antigen 125 is rising or clinical relapse is suspected.

Pancreatic Cancer

Current NCCN guidelines for pancreatic cancer (v.2.2021) state "the role of PET/CT (without iodinated intravenous contrast) remains unclear…[PET/CT] may be considered after formal pancreatic CT protocol in high-risk patients to detect extrapancreatic metastasis.[136.] It is not a substitute for high-quality, contrast-enhanced CT."

Penile Cancer

Current NCCN guidelines for penile cancer (v.2.2021) state that PET/CT may be considered for cross-sectional imaging of the chest/abdomen/pelvis for staging or treatment response assessment in patients with suspected inguinal lymph node positive disease. [139.]

Prostate Cancer

Current NCCN guidelines for prostate cancer (v.2.2021) indicate that ^{11}C-choline or ^{18}F-fluciclovine PET/CT or PET/MRI may be used for detection of biochemically recurrent small-volume disease in soft tissues and in bone. [156.]^{18}F-sodium fluoride PET/CT or PET/MRI may be considered for further bone assessment. Use of FDG-PET should not be used routinely for initial assessment or in other settings, due to limited evidence of clinical utility.

Renal Cell Carcinoma

Current NCCN guidelines for kidney cancer (v.1.2022) state that "The value of PET in RCC remains to be determined. Currently, PET alone is not a tool that is standardly used to diagnose kidney cancer or follow for evidence of relapse after nephrectomy."[166.]

Soft Tissue Sarcoma

Current NCCN guidelines for soft tissue sarcoma (v.2.2021) state that PET/CT may be useful in staging, prognostication, grading, and determining response to neoadjuvant therapy.[169.]PET/CT can be considered as a tool to help differentiate between well-differentiated and de-differentiated liposarcoma.

Testicular Cancer

Current NCCN guidelines for testicular cancer (v.2.2021) support the use of PET/CT to evaluate residual masses that are greater than 3 cm following primary treatment with chemotherapy (at ≥6 weeks posttreatment).[171.] If a PET/CT scan is negative, surveillance is recommended. If a PET/CT scan is positive, resection or biopsy of the residual mass is recommended. If the PET/CT scan results are indeterminate, then a repeat PET/CT is recommended in 6 to 8 weeks. Use of PET is not recommended for nonseminoma patients.

Thyroid Cancer

Differentiated

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The NCCN report conducted by Podoloff et al (2009) showed that PET can localize recurrent disease when other imaging tests are negative.[37.] Additionally, PET was found to be prognostic in this setting, showing that more metabolically active lesions on PET were strongly correlated with reduced survival.[174.]

Medullary

Current NCCN guidelines for thyroid carcinomas (v.1.2021) support use of FDG-PET/CT during disease monitoring for thyroid carcinomas when iodine-131 imaging is negative and stimulated thyroglobulin is greater than 2 to 5 ng/mL. For medullary thyroid cancer, Ga-68-dotatate PET/CT may be considered as part of the diagnostic workup, and recommend Ga-68-dotatate PET/CT or FDG-PET in certain cases for disease monitoring. Additionally, FDG-PET/CT may be considered as part of the diagnostic workup and as part of disease monitoring 3 to 6 months after initial therapy for anaplastic carcinoma.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Medicare National Coverage

Table 2. Medicare Coverage of FDG PET for Oncologic Conditions

Effective for claims with dates of service on and after June 11, 2013, the chart below summarizes national FDG PET coverage for oncologic conditions:

FDG PET for Cancers by Tumor Type	Initial Treatment Strategy (formerly "diagnosis" & "staging")	Subsequent Treatment Strategy (formerly "restaging" & "monitoring response to treatment")
Colorectal	Cover	Cover
Esophagus	Cover	Cover
Head and Neck (not thyroid, CNS)	Cover	Cover
Lymphoma	Cover	Cover
Non-small cell lung	Cover	Cover
Ovary	Cover	Cover
Brain	Cover	Cover
Cervix	Cover with exceptions *	Cover
Small cell lung	Cover	Cover
Soft tissue sarcoma	Cover	Cover
Pancreas	Cover	Cover
Testes	Cover	Cover
Prostate	**Non-cover**	Cover
Thyroid	Cover	Cover
Breast (male and female)	Cover with exceptions *	Cover
Melanoma	Cover with exceptions *	Cover
All other solid tumors	Cover	Cover
Myeloma	Cover	Cover
All other cancers not listed	Cover	Cover

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POLICY HISTORY - THIS POLICY WAS APPROVED BY THE FEP® PHARMACY AND MEDICAL POLICY COMMITTEE ACCORDING TO THE HISTORY BELOW:

Date	Action	Description
June 2012	New policy	
June 2013	Replace policy	Policy updated with literature review. References 22-35 added, Policy statements revised with NMN added to breast cancer, colorectal cancer, soft tissue sarcomas and thyroid cancer. Thyroid cancer revised to include both differentiated and poorly differentiated disease, Prostate cancer moved to section on Other Oncologic Applications, also added to this section, are diagnosis of brain tumors, restaging of gastric cancer, staging of multiple myeloma, evaluation of neuroendocrine tumors and staging of inguinal lymph nodes in patients with squamous cell carcinoma of the penis.
June 2014	Replace policy	Policy was revised with literature search adding references 37-40, 42-75. PET for gastric cancer as medically necessary for initial work up and staging and for evaluation of recurrent gastric cancer when other imaging modalities are inconclusive.
June 2015	Replace policy	Policy revised with literature review; references 1, 42-43, 46, 48-50, 58, 62, 72, 77, 84, and 87 added. Policy statements unchanged.
September 2017	Replace policy	Policy revised with literature review through March 23, 2017; references 37,41, 48-50, 59-63, 67, 69-70, 73, 76-80, 85, 94-98, 103, 109-110, 112, 115,119-120, and 126 added. Additional details added to policy statements. The following statements were changed to medically necessary: staging or restaging of brain cancer; evaluation of response to treatment in head and neck cancer; and testing with 11C-choline for evaluating response to primary treatment in prostate cancer. Two additional indications were added
December 2019	Replace policy	Policy revised with literature review through August 9, 2019; references on NCCN updated. Policy statements unchanged
December 2020	Replace policy	Policy revised with literature review through July 15, 2020; references added. Policy statements unchanged.
December 2021	Replace policy	Policy revised with literature review through August 5, 2021; references added. PET scanning for patients with suspected inguinal lymph node positive disease was added as medically necessary for staging patients. The following statements were revised to include newly approved radiotracers: "PET scanning with gallium 68 and copper 64 may be considered medically necessary as a technique for staging neuroendocrine tumors either during initial staging or for restaging at follow-up" and "PET scanning with gallium 68-prostate-specific membrane antigen and piflufolastat fluorine-18 is considered investigational in all aspects of managing prostate cancer."
June 2022	Replace policy	Policy revised with the following added to the Policy Objective and Prostate Cancer policy statement: PET scanning with Locametz specifically to select mCRPC patients for use of a targeted radioligand therapeutic agent (Pluvicto) is not currently addressed in this policy."

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