Medical Policy

BlueCross BlueShield Kansas
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Title: Positron Emission Tomography (PET) Scanning: (Genitourinary)

Related Policies:	▪ *PET Scanning- Oncologic Applications (Bone and Sarcoma)* ▪ *PET Scanning- Oncologic Applications (Brain, Melanoma, Unknown Primary)* ▪ *PET Scanning- Oncologic Applications (Breast and Gynecologic)* ▪ *PET Scanning- Oncologic Applications (Gastrointestinal and Pancreatic)* ▪ *PET Scanning- Oncologic Applications (Hematologic)* ▪ *PET Scanning- Oncologic Applications (Lung)* ▪ *PET Scanning: Miscellaneous (Non-cardiac, Non-oncologic) Applications of Fluorine 18 Fluorodeoxyglucose* ▪ *PET Scanning- Oncologic (Thyroid, Neuroendocrine, Head and Neck)*

Professional / Institutional
Original Effective Date: October 1, 1997 / September 11, 2004
Latest Review Date: January 13, 2026
Current Effective Date: January 13, 2026

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Populations	Interventions	Comparators	Outcomes
Individuals: • With suspected or diagnosed muscle-invasive bladder cancer and in need of staging or restaging information	Interventions of interest are: • 18F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity
Individuals: • Who are asymptomatic after completing muscle-invasive bladder cancer treatment	Interventions of interest are: • 18F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity
Individuals: • With suspected or diagnosed node negative penile cancer and in need of staging or restaging information	Interventions of interest are: • 18F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity
Individuals: • With suspected or diagnosed node positive penile cancer and in need of staging or restaging information	Interventions of interest are: • 18F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity
Individuals: • Who are asymptomatic after completing penile cancer treatment	Interventions of interest are: • 18F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity
Individuals: • With suspected or diagnosed prostate cancer and in need of staging or restaging information	Interventions of interest are: • ^{11}C-choline-PET, ^{11}C-choline-PET/CT, ^{18}F-fluciclovine-PET, or ^{18}F-fluciclovine-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity
Individuals: • Who are asymptomatic after completing prostate cancer treatment	Interventions of interest are: • ^{11}C-choline-PET, ^{11}C-choline-PET/CT, ^{18}F-fluciclovine-PET, or ^{18}F-fluciclovine-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity
Individuals:	Interventions of interest are:	Comparators of interest are:	Relevant outcomes include:

Populations	Interventions	Comparators	Outcomes
• With suspected prostate cancer	• 68Ga-PSMA PET, ^{68}Ga-PSMA PET/CT, piflufolastat-F^{18} PET, piflufolastat-F^{18} PET/CT, flotufolastat-F^{18} PET, and flotufolastat-F^{18} PET/CT	• Conventional imaging techniques	• Test validity
Individuals: • With diagnosed prostate cancer and in need of staging or restaging information	Interventions of interest are: • 68Ga-PSMA PET, ^{68}Ga-PSMA PET/CT, piflufolastat-F^{18} PET, piflufolastat-F^{18} PET/CT, flotufolastat-F^{18} PET, and flotufolastat-F^{18} PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity
Individuals: • Who are asymptomatic after completing prostate cancer treatment	Interventions of interest are: • 68Ga-PSMA PET, ^{68}Ga-PSMA PET/CT, piflufolastat-F^{18} PET, piflufolastat-F^{18} PET/CT, flotufolastat-F^{18} PET, and flotufolastat-F^{18} PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity
Individuals: • With diagnosed renal cell carcinoma and in need of staging or restaging information	Interventions of interest are: • 18F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity
Individuals: • With diagnosed testicular cancer and in need of staging or restaging information	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity
Individuals: • With suspected testicular cancer or who are asymptomatic after completing testicular cancer treatment	Interventions of interest are: • ^{18}F-FDG-PET or ^{18}F-FDG-PET/CT	Comparators of interest are: • Conventional imaging techniques	Relevant outcomes include: • Test validity

DESCRIPTION

Positron emission tomography (PET) is a nuclear imaging technique that uses positron-emitting tracers attached to molecules like glucose or water to create 3D images of metabolic activity. In cancer care, tracer choice depends on tumor type and cancer stage under evaluation.

The utility of PET scanning for the diagnosis, staging and restaging, and surveillance of malignancies varies by type of cancer. In general, PET scanning can distinguish benign from malignant masses in certain circumstances and improve the accuracy of staging by detecting additional disease not detected by other imaging modalities. Therefore, PET scanning for diagnosis and staging of malignancies can be considered medically necessary when specific criteria are met for specific cancers, as outlined in the policy statements. For follow-up, after initial diagnosis and staging have been performed, there are a few situations in which PET can improve detection of recurrence, and lead to changes in management that improve the net health outcome.

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 improves the net health outcome in individuals with genitourinary cancers.

BACKGROUND

Positron emission tomography (PET) is a nuclear imaging technique that uses positron-emitting tracers attached to molecules like glucose or water to create 3D images of metabolic activity. In cancer care, tracer choice depends on tumor type and cancer stage under evaluation.

REGULATORY STATUS

The following radiopharmaceuticals have been granted approval by the FDA, to be used with PET for genitourinary cancer-related indications (see Table 1).[1,]

Table 1. Radiopharmaceuticals Approved for Use With PET for Genitourinary 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
Fluorine-18 fluorodeoxyglucose (FDG)	Various		Suspected or existing diagnosis of cancer, all types

Radiopharmaceutical	Manufacturer	Name	Carcinoma-Related Indication With PET
Fluorine-18 fluciclovine	Blue Earth Diagnostics	Axumin™	Suspected prostate cancer recurrence based on elevated blood PSA levels after treatment
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
Flotufolastat fluorine-18	Blue Earth Diagnostics	Posluma®	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.

Three kits used for the preparation of Gallium-68 PSMA-11 have received FDA approval: the Illuccix® (Telix Pharmaceuticals) kit, approved in December 2021; the Locametz® (Advanced Accelerator Applications/Novartis) kit, approved in March 2022; and the Gozellix® (Telix Pharmaceuticals) kit, approved in March 2025.[2,] The preparation kits are for use in individuals with PSMA-positive prostate cancer with suspected metastasis who are candidates for initial definitive therapy, or with suspected recurrence based on elevated serum PSA level. In addition, Locametz is approved for selection of patients with metastatic prostate cancer, for whom lutetium Lu-177 vipivotide tetraxetan (Pluvicto™; Novartis) PSMA-directed therapy is indicated.

POLICY

- 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.

A. **Bladder Cancer**
   1. FDG-PET/CT 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.
   2. PET scanning is considered **experimental / investigational** for bladder tumors that have not invaded the muscle (stage < cT2).

B. **Penile Cancer**
   1. FDG-PET/CT scanning may be considered **medically necessary** for staging and restaging in individuals with suspected inguinal lymph node positive disease.
   2. PET scanning is considered **experimental / investigational** in all other aspects of managing penile cancer.

C. **Prostate Cancer**
   1. PET scanning with carbon 11 choline and fluorine 18 fluciclovine may be considered **medically necessary** for evaluating suspected or biochemically recurrent prostate cancer after primary treatment to detect small volume disease in soft tissues.
   2. PET/CT or PET/MRI scanning with gallium 68-prostate-specific membrane antigen, flotufolastat fluorine-18 and piflufolastat fluorine-18 may be considered **medically necessary** for any of the following applications:
      a. Individuals with diagnosed prostate cancer in need of staging information and:
         i. NCCN unfavorable intermediate-, high-, or very-high-risk prostate cancer (see Policy Guidelines); **OR**
         ii. NCCN unfavorable intermediate-, high-, or very-high-risk prostate cancer with equivocal results or oligometastatic disease on initial conventional imaging (see Policy Guidelines).
      b. Individuals with suspected recurrence of prostate cancer based on serum PSA level who have received:
         i. Radical prostatectomy with PSA level persistence or rise from undetectable level (see Policy Guidelines); **OR**
         ii. Definitive radiotherapy with PSA rise above nadir (see Policy Guidelines).
      c. Individuals with treated prostate cancer (including active surveillance/observation) in need of imaging as part of a workup for progression (see Policy Guidelines).
      d. Individuals with metastatic prostate cancer for whom lutetium Lu-177 vipivotide tetraxetan PSMA-directed therapy is indicated.
   3. Use of gallium 68-prostate-specific membrane antigen, flotufolastat fluorine-18 and piflufolastat fluorine-18 in known or suspected prostate cancer is considered **experimental / investigational** for all other indications, including diagnosis,

primary staging of very-low, low- or favorable intermediate-risk prostate cancer, and evaluation of response to therapy.

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

D. **Renal Cell Carcinoma**

1. FDG-PET or FDG-PET/CT scanning is considered **experimental / investigational** in all aspects of managing renal cancer.

E. **Testicular Cancer**

1. FDG-PET or FDG-PET/CT 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.)
2. Except as noted above for seminoma, PET scanning is considered **experimental / investigational** in evaluation of testicular cancer, including but not limited to the following applications:
   a. Initial staging of testicular cancer
   b. Distinguishing between viable tumor and necrosis/fibrosis after treatment of testicular cancer, and
   c. Detection of recurrent disease after treatment of testicular cancer

F. **Cancer Surveillance**

1. PET scanning is considered **experimental / investigational** when used as a surveillance tool for individuals 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 individuals without objective signs or symptoms suggestive of cancer recurrence (see Policy Guidelines section).

POLICY GUIDELINES

A. For this policy, PET scanning is discussed for the following 4 applications in oncology.

1. Diagnosis
   Diagnosis refers to use of PET as part of the testing used in establishing whether a patient has cancer.
2. Staging
   Staging refers to use of PET to determine the stage (extent) of the cancer at the time of diagnosis before any treatment is given. Imaging at this time is generally to determine whether the cancer is localized. This may also be referred to as initial staging.
3. Restaging
   Restaging refers to imaging after treatment in 2 situations.
   a. Restaging is part of the evaluation of a patient in whom a disease recurrence is suspected based on signs and/or symptoms.
   b. Restaging also includes determining the extent of malignancy after completion of a full course of treatment.
4. Surveillance
   Surveillance refers to the use of imaging in asymptomatic patients (patients without objective signs or symptoms of recurrent disease). This imaging is completed 6 months or more (≥12 months for lymphoma) after completion of treatment.

B. **Prostate-Specific Membrane Antigen Positron Emission Tomography**
Appropriate selection of patients for prostate-specific membrane antigen (PSMA) PET imaging may be guided according to National Comprehensive Cancer Network (NCCN) and Society of Nuclear Medicine and Molecular Imaging (SNMMI) criteria (see policy section ^{68}Ga-PSMA PET, ^{68}Ga-PSMA PET/CT, Piflufolastat-F^{18} PET, and Piflufolastat-F^{18} PET/CT Guidelines). NCCN and SNMMI recommendations for use of PSMA PET in individuals with newly diagnosed prostate cancer in need of staging are based on the following NCCN risk criteria:

Risk Group	**Clinical/Pathological Features**
Very Low	Has all of the following: • cT1c • Grade Group 1 • PSA <10 ng/mL • Fewer than 3 prostate biopsy fragments/cores positive, ≤50% cancer in each fragment/core • PSA density <0.15 ng/mL/g
Low	Has all of the following but does not qualify for very low risk: • cT1–cT2a • Grade Group 1 • PSA <10 ng/mL
Intermediate	• Has all of the following: • No high-risk group features • No very-high-risk group features • Has one or more intermediate risk factor: • cT2b–cT2c • Grade Group 2 or 3 • PSA 10–20 ng/mL
Favorable Intermediate	Intermediate risk criteria, AND all of the following: • 1 intermediate risk factor • Grade Group 1 or 2 • <50% biopsy cores positive (e.g., <6 of 12 cores)
Unfavorable Intermediate	Intermediate risk criteria AND one or more of the following: • 2 or 3 intermediate risk factors • Grade Group 3 • ≥50% biopsy cores positive (e.g., ≥6 of 12 cores)
High	Has no very-high-risk features and has exactly one high-risk feature: • cT3a OR • Grade Group 4 or Grade Group 5 OR • PSA >20 ng/mL
Very High	Has at least one of the following: • cT3b– cT4 • Primary Gleason pattern 5 • 2 or 3 high-risk features • >4 cores with Grade Group 4 or 5

Individuals who meet unfavorable intermediate-, high- and very-high risk criteria are suitable candidates for PSMA PET bone and/or soft tissue imaging, either following equivocal results on initial conventional imaging (e.g., MRI) or as alternative to conventional imaging.

PSMA PET imaging is not recommended for staging newly diagnosed individuals in very low, low, or favorable intermediate NCCN risk groups, or for individuals with suspected prostate cancer based on elevated PSA, increasing PSA on serial measurements, and/or clinical signs (e.g., abnormal digital rectal exam).

Use of PSMA PET imaging is appropriate for individuals who have undergone radical prostatectomy or radiation therapy for prostate cancer with subsequent suspected persistence or recurrence. Specific considerations for use of PSMA PET are:

- Following radical prostatectomy AND:
  - Failure of PSA to fall to undetectable levels; OR
  - Previously undetectable PSA with a subsequent detectable PSA that increases on ≥2 measurements
- Following definitive radiation therapy AND:
  - A PSA rise ≥2 ng/mL above the nadir; OR
  - A positive digital rectal exam.

PSMA PET may also be considered when PSA has been confirmed to be increasing after radiation therapy even if the increase above nadir is not yet 2 ng/mL, particularly in candidates with a favorable prognosis for salvage local therapy.

PSMA PET use is appropriate in individuals who have previously been treated for prostate cancer (including those under active surveillance/observation) who require imaging as part of a workup for progression. NCCN guidelines include recommended workup protocols, which vary according to prior treatment and cancer stage. The guidelines recommend use of PSMA PET bone and soft tissue imaging when conventional imaging results are equivocal, but also state that PSMA PET imaging is more accurate than conventional imaging at detecting micrometastatic disease, and as such, the guidelines note that conventional imaging is not a necessary prerequisite to PSMA PET imaging.

Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

RATIONALE

This evidence review was created using searches of the PubMed database. The most recent literature update was performed through October 20, 2025.

The review has been informed by multiple evaluations of positron emission tomography (PET), including TEC Assessments, other systematic reviews, meta-analyses, and decision analyses.

Evidence reviews assess whether a medical test is clinically useful. A useful test provides information to make a clinical management decision that improves the net health outcome. That

is, the balance of benefits and harms is better when the test is used to manage the condition than when another test or no test is used to manage the condition.

The first step in assessing a medical test is to formulate the clinical context and purpose of the test. The test must be technically reliable, clinically valid, and clinically useful for that purpose. Evidence reviews assess the evidence on whether a test is clinically valid and clinically useful. Technical reliability is outside the scope of these reviews, and credible information on technical reliability is available from other sources.

POSITRON EMISSION TOMOGRAPHY AND POSITRON EMISSION TOMOGRAPHY PLUS COMPUTED TOMOGRAPHY

Clinical Context and Test Purpose

PET and PET combined with CT or MRI are used in oncology for diagnosis, staging, restaging, and surveillance. Diagnostic use of PET aids in distinguishing between benign and malignant processes. Initial staging assesses the extent and location of cancer before treatment. Restaging reevaluates cancer after treatment depending on tumor and treatment approach to establish a post-treatment baseline, or over timer when recurrence is suspected. Surveillance involves imaging patients without objective signs or symptoms of recurrent disease (altered symptoms) or with stable symptoms, generally six months or more after treatment.

The following PICO was used to select literature to inform this review.

Populations

The relevant populations of interest are:

- Individuals who are suspected of having genitourinary cancer.
- Individuals diagnosed with genitourinary cancer and need information on the extent of cancer (initial staging upon diagnosis confirmation or restaging following treatment).
- Individuals with genitourinary cancer who have completed a round of treatment and may be at risk of recurrence.

Interventions

The test being considered is PET or PET/CT. A PET scan is a nuclear medicine 3-dimensional imaging technique. Radioactive tracers are ingested or injected, and radioactive emissions are detected by an imaging device, allowing observations on blood flow, oxygen use, and metabolic processes around the lesions. When CT is added to PET, the images are superimposed, providing additional anatomic information. The most common radioactive tracer used for oncologic applications is fluorine 18 (^{18}F) fluorodeoxyglucose (FDG). Radiation exposure from PET and PET/CT is considered moderate to high.

Comparators

The comparators of interest are conventional imaging techniques such as ultrasound, magnetic resonance imaging (MRI), and x-rays.

Outcomes

The general outcomes of interest are related to the clinical validity of PET, PET/CT, or PET/MRI in (1) diagnosing suspected cancer, (2) providing staging or restaging information, and (3) detecting recurrence following cancer treatment. Clinical validity is most often measured by

sensitivity, specificity, positive predictive values (PPV), and negative predictive values (NPV). For the clinical utility of PET, PET/CT, or PET/MRI to be demonstrated, the tests would need to inform treatment decisions that would improve survival and quality of life.

Study Selection Criteria
Methodologically credible studies were selected using the following principles:

- To assess the clinical validity of PET and PET/CT, studies should report sensitivity, specificity, PPV, and NPV. Additionally, studies reporting false-positive rates and false-negative rates are informative.
- To assess the clinical utility of PET and PET/CT, studies should demonstrate how results of these imaging techniques impacted treatment decisions and overall management of the patient.

Clinically Valid
A test must detect the presence or absence of a condition, the risk of developing a condition in the future, or treatment response (beneficial or adverse).

Clinical validity can be measured by comparing results from PET, PET/CT, or PET/MRI with results from conventional imaging techniques.

Clinically Useful
A test is clinically useful if the use of the results informs management decisions that improve the net health outcome of care. The net health outcome can be improved if individuals receive correct therapy or more effective therapy, avoid unnecessary therapy, or avoid unnecessary testing.

Ideally, outcomes for clinical utility would reflect long-term patient status, which, depending on the type of cancer, can range from months to years. To practically assess the clinical utility of PET, PET/CT or PET/MRI, studies should demonstrate how results of these imaging techniques impacted treatment decisions and overall management of the patient.

Direct Evidence
Direct evidence of clinical utility is provided by studies that have compared health outcomes for individuals managed with and without the test. Because these are intervention studies, the preferred evidence would be from randomized controlled trials (RCTs).

Chain of Evidence
Indirect evidence on clinical utility rests on clinical validity. If the evidence is insufficient to demonstrate test performance, no inferences can be made about clinical utility.

PET scan research in oncology primarily addresses sensitivity and specificity through reviews and meta-analyses. Studies on changes to staging or treatment are limited but do report improved tumor type specific health outcomes. Following evidence-based clinical guidelines may enhance net health outcomes by improving therapeutic effectiveness, reducing unnecessary tests, treatments, or adverse events.

REVIEW OF EVIDENCE

BLADDER CANCER

Systematic Reviews

A systematic review and meta-analysis (25 studies, N=1656) by Abdlkadir et al (2025) evaluated the diagnostic performance of FDG-PET/CT and PET/MRI for preoperative locoregional staging of urinary bladder cancer.[3,] For primary tumor detection, pooled per-patient detectability was 69% (95% CI, 53% to 84%; I^2=44%) across 5 PET/CT studies (n=141) with no significant heterogeneity, while 3 PET/MRI studies (n=80) yielded 90% (95% CI, 67%to 100%; I^2=10%) with no significant heterogeneity; an indirect comparison favored PET/MRI (indirect OR, 3.1; 95% CI, 1.5 to 7.7). For pelvic lymph-node staging, 18 PET/CT studies (N=1,505) showed pooled sensitivity 50% (95% CI, 41% to 58%; I^2=85%; p=.00001) and specificity 91% (95% CI, 87% to 94%; I^2=67%; p=.0001), with positive likelihood ratio 5.7 (95% CI, 3.8 to 8.7; I^2=53%; p=.004), negative likelihood ratio 0.6 (95% CI, 0.5 to 0.7; I^2=61%; p=.0002), and diagnostic odds ratio 10 (95% CI, 6 to 18; I^2=54%; p=.004). Study quality was assessed using QUADAS-2, and several studies revealed a high risk of bias in patient selection, with additional concerns regarding incomplete index-test reporting and uncertainty in the reference standard.

GUIDELINES

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 (2.2025) 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. 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.

Section Summary: Bladder Cancer
Evidence for the use of FDG-PET and FDG-PET/CT for the diagnosis and for the staging and restaging of muscle-invasive bladder cancer consists of a systematic review and meta-analysis of several studies. Pooled analyses have shown that PET/CT is effective in the staging of muscle-invasive bladder cancer. The evidence supports the use of FDG-PET/CT for the diagnosis and staging and restaging of muscle-invasive bladder cancer.

The evidence does not support the use of FDG-PET/CT for nonmuscle invasive bladder cancer. The evidence does not support the use of FDG-PET, ^{18}F-FET-PET, and ^{11}C-methionine PET for surveillance of brain tumors.

PENILE CANCER

Systematic Reviews
Lee et al (2022) conducted a systematic review and meta-analysis of 5 prospective and 7 retrospective cohort studies (12 studies; N=479) published through August 2021 on the diagnostic accuracy of FDG-PET/CT for lymph node staging in penile cancer.[6,] Histopathological analysis was the reference standard in all included studies; direct comparison of FDG-PET/CT with other imaging modalities was not reported. Most studies had low or unclear risk of bias across QUADAS-2 domains, and Deek's test for publication bias was not significant (p=.45). FDG-PET/CT was associated with a pooled sensitivity of 87% (95% CI, 79% to 92%) and a pooled specificity of 88% (95% CI, 79% to 93%). Heterogeneity was present for both sensitivity (I^2=68%) and specificity (I^2=85%) and meta-regression analysis could not account for the heterogeneity. The analysis found a positive likelihood ratio of 7.2 (95% CI 3.9 to 13.1) and a negative likelihood ratio of 0.15 (95% CI 0.10 to 0.24). The pooled diagnostic odds ratio was 47 (95% CI, 19 to 116) and the AUC was 0.93 (95% CI, 0.90 to 0.95). Subgroup analysis of diagnostic accuracy stratified according to inguinal or pelvic lymph nodes found similar sensitivities (84% and 89%) and specificities (79% and 83%) with no difference between groups in AUC (area difference -0.044; p=.34). Although the review showed that FDG-PET/CT had good diagnostic capability, this study is limited by the heterogeneity among the studies and the lack of comparison with other imaging modalities.

Comparative Studies
Jakobsen et al (2021) retrospectively evaluated the diagnostic accuracy of FDG-PET/CT compared to contrast-enhanced CT in the assessment of inguinal lymph node status, distant metastases

and synchronous cancer at 2 medical centers.[7,]ndividuals diagnosed with invasive penile squamous cell carcinoma who received a preoperative FDG-PET/CT were included. A radiologist, blinded to FDG-PET/CT results, analyzed and interpreted the CT part of the scan for suspicious findings. There were 171 individuals evaluated for distant metastases and synchronous incident cancers. Additionally, there were 286 groins in 143 individuals evaluated for lymph node metastases. For detection of lymph node metastases, 6 of the 171 groins read as negative by FDG-PET/CT were false positives (false negative rate of 11.5% per groin). For the diagnostic accuracy for inguinal lymph node status, with histopathology or complete clinical follow-up as reference, FDG PET/CT sensitivity and specificity was 85.4% and 57.8% per patient, respectively. For CT, sensitivity and specificity was 47.5% and 95.8% per patient, respectively.

Guidelines
Current NCCN guidelines for penile cancer (v. 2.2025) state that PET/CT may be considered for cross-sectional imaging of the chest/abdomen/pelvis for staging or treatment response assessment in individuals with suspected inguinal lymph node positive disease. PET/CT can also be used to evaluate enlarged pelvic lymph nodes if percutaneous lymph node biopsy is not technically feasible.[8,]

Section Summary: Penile Cancer
Evidence for the use of PET or PET/CT in the management of individuals with penile cancer consists of a systematic review and a retrospective comparative study. In individuals with suspected inguinal lymph node positive disease, PET/CT may offer increased sensitivity compared to CT alone for staging. Current NCCN guidelines note that PET/CT can be considered for staging or treatment response assessment in individuals with node positive disease.

The evidence does not support the use of FDG-PET and FDG-PET/CT for the diagnosis, staging, restaging, or surveillance of node negative penile cancer.

The evidence does support the use of FDG-PET and FDG-PET/CT for the staging and treatment response assessment of node positive penile cancer.

The evidence does not support the use of FDG-PET and FDG-PET/CT for the diagnosis or surveillance of node positive penile cancer.

PROSTATE CANCER

^{11}C-CHOLINE PET, ^{11}C-CHOLINE PET/CT, ^{18}F-FLUCICLOVINE PET

Prostate Cancer Diagnosis
Liu et al (2016) and Ouyang et al (2016) conducted meta-analyses comparing the diagnostic accuracy of 4 radiotracers (FDG, carbon 11 choline [^{11}C-choline], fluorine 18 fluorocholine [^{18}F-FCH], and carbon 11 acetate [^{11}C-acetate]) in detecting prostate cancer.[9,10,] The literature search for the Liu review, conducted through July 2015, identified 56 studies (N=3586) for inclusion. Using the QUADAS-2 system to evaluate study quality, reviewers determined that the studies were reliable, with scores of 6 to 9 out of 10. Pooled estimates for the 4 types of radiotracers are summarized below (see Table 8). The literature search for the Ouyang et al (2016) review included studies using elastography and was conducted through April 2015. Study quality was not addressed.

Biscontini et al (2021) conducted a meta-analysis to evaluate the diagnostic accuracy of ^{18}F-fluciclovine for the diagnosis of primary cancer, pre-operative lymph node staging, detection of recurrent disease, and for bone metastasis assessment.[11,] Fifteen studies (N=697) were evaluated: 6 studies for diagnosis, 3 for staging, 6 for recurrence of disease, and 1 for evaluation of bone metastasis. Pooled estimates for diagnosis are included in Table 8.

Table 8. Pooled Diagnostic Performance of Different Radiotracers in Detecting Prostate Cancer

Imaging Technique	No. of Studies	Sensitivity % (95% CI)	Specificity % (95% CI)	AUC (95% CI)
Liu et al (2016)[9,]				
^{11}C-choline PET/CT	31	81 (77 to 88)	82 (73 to 88)	0.89 (0.86 to 0.91)
^{18}F-FCH-PET/CT	15	76 (49 to 91)	93 (84 to 97)	0.94 (0.92 to 0.96)
^{11}C-acetate PET/CT	5	79 (70 to 86)	59 (43 to 73)	0.78 (0.74 to 0.81)
FDG-PET/CT	5	67 (55 to 77)	72 (50 to 87)	0.73 (0.69 to 0.77)
Ouyang et al (2016)[10,]				
Elastography[a]	26	76 (68 to 83)	78 (72 to 83)	0.84 (NR)
^{11}C-choline PET/CT	31	78 (72 to 84)	79 (71 to 82)	0.85 (NR)
^{18}F-FCH-PET/CT	15	73 (54 to 87)	59 (41 to 75)	0.91 (NR)
^{11}C-acetate PET/CT	5	79 (68 to 86)	59 (41 to 75)	0.77 (NR)
FDG-PET/CT	5	76 (68 to 83)	78 (72 to 83)	0.84 (NR)
Biscontini et al (2021)[11,]				
^{18}F-fluciclovine	6	83 (80 to 86)	77 (74 to 80)	0.92 (NR)

11C-acetate: carbon 11 acetate; 11C-choline: carbon 11 choline; 18F-FCH: fluorine 18 fluorocholine; AUC: area under the curve; CI: confidence interval; CT: computed tomography; FDG: fluorine 18 fluorodeoxyglucose; NR: not reported; PET: positron emission tomography.
[a] Includes transrectal real-time elastosonography and shear-wave elastography.

PROSTATE CANCER STAGING AND RESTAGING

Systematic Reviews

The meta-analysis by Biscontini et al (2021), described previously, assessed the accuracy of ^{18}F-fluciclovine.[11,] For pre-operative lymph node staging (3 studies), the pooled sensitivity and specificity was 57% (95% CI, 39% to 73%) and 99% (95% CI, 94% to 100%), respectively. For the detection of recurrent disease (6 studies), the pooled sensitivity and specificity was 68% (95% CI, 63% to 73%) and 68% (95% CI, 60% to 75%), respectively.

A meta-analysis by Fanti et al (2016) assessed the accuracy of ^{11}C-choline PET/CT in the restaging of individuals with prostate cancer with biochemical recurrence after initial treatment with curative intent.[12,] The literature search, conducted through December 2014, identified 12

studies (N =1270) for inclusion in the analysis. Pooled sensitivity and specificity were 89% (95% CI, 83% to 93%) and 89% (95% CI, 73% to 96%), respectively.

In a meta-analysis by von Eyben and Kairemo (2014), the pooled sensitivity and specificity of ^{11}C-choline PET/CT for detecting prostate cancer recurrence in 609 individuals were 62% (95% CI, 51% to 66%) and 92% (95% CI, 89% to 94%), respectively.[13,] In an evaluation of 280 individuals from head-to-head studies comparing choline PET/CT with bone scans, PET/CT identified metastases significantly more often than did bone scanning (127 [45%] vs 46 [16%], respectively; OR, 2.8; 95% CI, 1.9 to 4.1; p<.001). Reviewers also reported that ^{11}C-choline PET/CT changed treatment in 381 (41%) of 938 individuals. Complete prostate-specific antigen (PSA) response occurred in 101 (25%) of 404 individuals.

A systematic review by Umbehr et al (2013) investigated the use of ^{11}C-choline and ^{18}F-FCH-PET and ^{18}F-FCH-PET/CT in staging and restaging of prostate cancer. The literature search, conducted through July 2012, identified 10 studies (N=637) to be included in the initial prostate cancer staging analysis; pooled sensitivity was 84% (95% CI, 68% to 93%) and specificity was 79% (95% CI, 53% to 93%).[14,] Twelve studies (N=1055) were included in the restaging analysis; pooled sensitivity and specificity were 85% (95% CI, 79% to 89%) and 88% (95% CI, 73% to 95%), respectively.

Mohsen et al (2013) conducted a systematic review of 23 studies on ^{11}C-acetate PET imaging for the detection of primary or recurrent prostate cancer.[15,] For detection of recurrence, 14 studies were included in a meta-analysis. The pooled sensitivity was 68% (95% CI, 63% to 73%) and pooled specificity was 93% (95% CI, 83% to 98%). Study quality was considered poor, and low sensitivities and specificities appear to limit the validity of ^{11}C-acetate imaging in prostate cancer. Currently, ^{11}C-acetate is not approved by the U.S. Food and Drug Administration.

Other systematic reviews, including those by Sandgren et al (2017) and Albisinni et al (2018), have also reported that ^{11}C-choline PET/CT exhibits high sensitivity and specificity estimates in the staging and restaging of prostate cancer.[16,17,]

Prostate Cancer Management

Jani et al (2021) conducted a single-center, open-label, phase 2/3 randomized controlled trial that evaluated the benefit of ^{18}F-fluciclovine-PET/CT in individuals who had undergone radical prostatectomy and were experiencing biochemical recurrence to guide final radiotherapy treatment decisions.[18,]ndividuals were randomly assigned in a 1:1 ratio to radiotherapy directed by conventional imaging only, or to radiotherapy directed by conventional imaging plus ^{18}F-fluciclovine-PET/CT. All 81 individuals in the conventional imaging group received radiotherapy (56 to prostate bed alone and 25 to prostate bed and pelvic nodes). In the ^{18}F-fluciclovine-PET/CT group, 76 (95%) of the 80 individuals received radiotherapy (41 to the prostate bed alone and 35 to the prostate bed and pelvic nodes). Median follow-up for the whole cohort was 3.52 years. Median survival was not reached in both groups. Three-year event-free survival was 63% (95% CI, 49.2 to 74) in the conventional imaging group compared with 75.5% (95% CI, 62.5 to 84.6 in the ^{18}F-fluciclovine-PET/CT group (difference, 12.5 percentage points [95% CI, 4.3 to 20.8]; p=.0028).

Dreyfuss et al (2021) conducted a single-center retrospective evaluation of individuals with biochemical recurrence after primary treatment for prostate cancer who received imaging

with ^{18}F-fluciclovine-PET/CT.[19,] A total of 328 individuals were included resulting in 336 ^{18}F-fluciclovine PET/CT scans, which were classified as positive (65%), negative (25%), or equivocal (10%) based on radiology reports. Sensitivity and specificity were 93% (95% CI, 86% to 96%) and 63% (95% CI, 45% to 77%), respectively, using biopsy and other imaging as the reference standard. Management recommendations after imaging was only available for 241 scans (72%). Of the evaluable scans, 73% had management changes with ^{18}F-fluciclovine-PET/CT data with 58% of those recommendations involving treatment modality decisions.

Andriole et al (2018) presented results from the LOCATE trial.[20,] The study population consisted of 213 men who had undergone curative-intent treatment of histologically confirmed prostate cancer and were suspected to have recurrence based on rising PSA levels. Fluciclovine-avid lesions were detected in 122 (57%) individuals. Compared with management plans specified by the treating physicians prior to the PET scans, 126 (59%) individuals had a change in management. The most frequent change in management was from salvage or noncurative systemic therapy to watchful waiting (n=32) and from noncurative systemic therapy to salvage therapy (n=30).

Akin-Akintayo et al (2017) evaluated the role of fluciclovine PET/CT in the management of post-prostatectomy individuals with PSA failure being considered for salvage radiotherapy.[21,] Forty-two individuals who were initially planning radiotherapy due to post-prostatectomy PSA failure underwent fluciclovine PET/CT. Based on the PET/CT results, 17 (40.5%) individuals changed a decision relating to the radiotherapy: 2 individuals received hormonal therapy rather than radiotherapy when fluciclovine showed extrapelvic disease; 11 individuals increased the radiotherapy field from prostate bed only to prostate plus pelvis, and 4 individuals reduced the radiotherapy fields from prostate plus pelvis to prostate bed only.

In a meta-analysis of 14 studies (N=1667) of radiolabeled choline PET/CT for restaging prostate cancer, Treglia et al (2014) reported a maximum pooled sensitivity of 77% (95% CI, 71% to 82%) in individuals with a PSA velocity of greater than 2 ng/mL per year.[22,] Pooled sensitivity was lower for individuals with a PSA velocity of less than 2 ng/mL per year or with a PSA level doubling time of 6 months or less. In meta-analysis of 11 studies (N=609) of radiolabeled choline PET/CT for staging or restaging prostate cancer, von Eyben et al (2014) reported a pooled sensitivity and specificity of 59% (95% CI, 51% to 66%) and 92% (95% CI, 89% to 94%), respectively.[13,] Pooled PPV and NPV were 70% and 85%, respectively.

GUIDELINES

American College of Radiology

In 2018, the ACR published an Appropriateness Criteria on the posttreatment follow-up of individuals with prostate cancer stating that PET and PET/CT using ^{11}C-choline or ^{18}F-fluciclovine radiotracers is usually appropriate for individuals with a clinical concern for residual or recurrent disease following radical prostatectomy, nonsurgical treatments, or systemic therapy.[23,]

American Urological Association et al

Practice guidelines from the American Urological Association/American Society for Radiation Oncology/Society of Urologic Oncology (2021) recommend CT or MRI for cross-sectional imaging, along with bone scintigraphy, as the standard imaging approach for the post-treatment biochemical recurrence after exhaustion of local treatment.[24,] Novel PET tracers (^{11}C-choline, ^{18}F-

fluciclovine, prostate-specific membrane antigen [PSMA]-targeting radiotracers) "appear to show greater sensitivity than conventional imaging for the detection of prostate cancer recurrence and metastases at low PSA values (<2.0 ng/mL)." However, the guideline notes that it is unclear what clinical benefits and impact on OS is achieved with earlier detection of recurrent disease, and that "to date there is only evidence that it may delay initiation of systemic therapy. There is no evidence yet that metastasis directed therapy confers a survival benefit."

National Comprehensive Cancer Network
Current NCCN guidelines for prostate cancer (2.2026) 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.[25,18]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 due to limited evidence of clinical utility.

Society of Nuclear Medicine and Molecular Imaging
The Society of Nuclear Medicine and Molecular Imaging (SNMMI) published appropriate use criteria (2020) on evaluation of men with biochemical recurrence of prostate cancer after definitive primary therapy with radical prostatectomy or radiotherapy.[26,] For those with negative or equivocal results on initial standard imaging, ^{11}C-choline or ^{18}F-fluciclovine PET/CT are considered appropriate to use.

Subsection Summary: ^{11}C-Choline PET, ^{11}C-Choline PET/CT, ^{18}F-Fluciclovine PET, and ^{18}F-Fluciclovine PET/CT for Prostate Cancer
Evidence for the use of ^{11}C-choline PET, ^{11}C-choline PET/CT, ^{18}F-fluciclovine PET, and ^{18}F-fluciclovine PET/CT for diagnosis, staging, and restaging of prostate cancer, consists of meta-analyses, which have shown that the 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. 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 supports the use of ^{11}C-choline PET and PET/CT and ^{18}F-fluciclovine PET and PET/CT for the diagnosis, staging, and restaging of prostate cancer.

The evidence does not support the use of ^{11}C-choline PET and PET/CT and ^{18}F-fluciclovine PET and PET/CT for surveillance of prostate cancer.

^{68}Ga-PSMA PET, ^{68}Ga-PSMA PET/CT, Piflufolastat-F^{18} PET, Piflufolastat-F^{18} PET/CT, Flotufolastat-F^{18} PET, and Flotufolastat-F^{18} PET/CT
FDA-approved PSMA-targeting radiotracers for PET include ^{68}Ga PSMA, piflufolastat-F^{18}, and flotufolastat-F^{18}. The Albisinni et al (2018) review, discussed in the ^{11}C-choline PET/CT section, and a systematic review by Eissa et al (2018) noted that an advantage of using PSMA-targeting radiotracers compared with ^{11}C-choline and ^{18}F-fluciclovine is the potential to detect local and distant recurrences in individuals with lower PSA levels.[17,27,]

Prostate Cancer Diagnosis
Kawada et al (2022) conducted a systematic review on the diagnostic accuracy of PSMA PET for detection of clinically significant prostate cancer.[28,] Five studies reporting data from 497

individuals with suspected prostate cancer due to elevated PSA were included in the review; 2 studies included only biopsy-naïve individuals (N=333) while in the remaining 3 studies participants had a prior negative biopsy. The median pre-imaging PSA was 8.0 ng/mL (range, 5.6 to 18 ng/mL). The prevalence of clinically significant prostate cancer, variably defined among the studies but generally requiring an International Society of Urologic pathology grade group ≥2, was 59% (range, 32% to 75%). ^{68}GA was the imaging agent in 4 of the studies. Three of the studies (N=228) assessed PSMA PET, MRI, and PSMA PET/MRI and reported diagnostic measures for all 3 imaging modalities. In all studies, systemic and targeted biopsy was the reference standard. Risk of bias, assessed using the QUADAS-2 tool, was judged to be low in one study and moderate in the other studies.

Measures of diagnostic accuracy are reported in Table 9. Results were similar for PSMA PET and MRI, alone and in combination, with overlapping CIs, and were consistent when limited to 2 studies of biopsy-naïve individuals.

Table 9. Diagnostic Performance of Imaging Modalities in Detecting Clinically Significant Prostate Cancer

Imaging Technique for Targeted Biopsy	No. of Studies	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	DOR (95% CI)	AUC
Kawada et al 2022[28,]							
All studies PSMA PET	5	89 (85 to 93)	56 (29 to 80)	69 (58 to 79)	78 (50 to 93)	10.50 (2.59 to 42.57)	0.88
Studies comparing imaging techniques PSMA PET	3	90 (85 to 93)	39 (14 to 71)	68 (62 to 73)	72 (29 to 94)	5.16 (1.07 to 24.79)	0.88
MRI	3	84 (78 to 88)	53 (46 to 60)	70 (46 to 87)	76 (55 to 89)	6.40 (4.00 to 10.32)	0.81
PSMA PET/MRI	3	91 (77 to 97)	64 (40 to 82)	75 (56 to 87)	85 (62 to 95)	19.04 (9.54 to 38.02)	0.87

AUC: area under the curve; DOR: diagnostic odds ratio; MRI: magnetic resonance imaging; NPV: negative predictive value; PET: positron emission tomography; PPV: positive predictive value; PSMA: prostate-specific membrane antigen.

Prostate Cancer Staging

Stabile et al (2022)[29,] and Wang et al (2021)[30,] conducted systematic reviews on the use of PSMA PET for prostate cancer staging.

The Stabile review included 27 studies (N=2832) assessing the diagnostic accuracy of PSMA PET/CT for prostate cancer staging in newly diagnosed individuals. Specifically, studies were included that reported on the predictive ability of PSMA PET for lymph node invasion. The mean PSA at baseline, reported in 14 studies, was 12.2 ng/mL. Among the studies, 9 included high-risk

individuals, 1 included intermediate-risk individuals, 15 included individuals with mixed risk levels, and 2 did not report risk. ^{68}GA was the imaging agent used in 22 of the studies. The reference standard was pelvic lymph node dissection in all of the included studies. Risk of bias was assessed using QUADAS-2 criteria; nearly all the studies had limitations resulting in unclear or high risk of bias ratings for 1 or more QUADAS-2 domain. Funnel plots and Egger's test found potential publication bias for sensitivity (p=.002) and negative predictive value (p=.02), but not for specificity (p=.1) or positive predictive value (p=.1).

Measures of diagnostic accuracy are reported in Table 10. Among the studies, the median prevalence of lymph node invasion was 26% (interquartile range [IQR], 20% to 34%; range 5% to 58%). Higher prevalence was associated with a significant decrease in negative predictive value (p=.04). Study authors stated that the clinical implication of these findings suggested that for individuals with a nomogram-calculated borderline risk of lymph node invasion and negative PSMA PET/CT, avoidance of pelvic lymph node dissection might be considered, while in individuals with higher-risk prostate cancer, avoidance of pelvic lymph node dissection should not be considered due to the decreased NPV in this risk group.

Wang et al (2021)[30,] conducted a systematic review of 9 studies (N=640) comparing the diagnostic accuracy of ^{68}GA PSMA PET/CT with multiparametric MRI for lymph node staging prior to prostatectomy in individuals with intermediate or high-risk prostate cancer. The reference standard was pelvic lymph node dissection. The median prevalence of pelvic lymph node metastases was 25% (range, 4% to 58%). The median PSA ranged widely among 6 studies from 7.4 to 37.3 ng/mL and was not reported in the other 3 studies. Eight studies were retrospective, and the other was prospective; QUADAS-2 assessment of study quality found the majority of studies had low or unclear risk of bias for most domains. No publication bias was found for either ^{68}GA PSMA PET/CT (p=.15) or multiparametric MRI (p=.87). Study results are summarized in Table 10. Sources of heterogeneity based on meta-regression analysis included pelvic lymph node metastases prevalence, PSA level, risk group, and reference standard for ^{68}GA PSMA PET/CT and number of patients and PSA level for multiparametric MRI.

Table 10. Diagnostic Performance of Imaging Modalities for Prostate Cancer Staging

	No. of Studies	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	DOR (95% CI)	AUC (95% CI)
Stabile et al (2022)[29,]							
PSMA PET Overall	27	58 (50 to 66)	95 (93 to 97)	79 (72 to 85)	87 (84 to 89)	14.76 (to 19.00)	0.84 (0.87 to 0.81)
High-risk	9	54 (37 to 70)	95 (91 to 98)	77 (67 to 86)	83 (79 to 87)	18.97 (10.65 to 33.78)	-
Intermediate-risk	1	93 (76 to 100)	96 (86 to 100)	93 (76 to 100)	96 (86 to 100)	364 (21.12 to 6273)	-
Mixed-risk	15	58 (49 to 67)	94 (92 to 96)	77 (68 to 85)	88 (84 to 91)	13.58 (9.98 to 18.47)	-

	No. of Studies	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	DOR (95% CI)	AUC (95% CI)
p value for between risk group difference	-	.008	.9	.3	.04		
Wang et al (2021)[30,]							
PSMA PET	9	71 (48 to 86); I^2=75%	92 (88 to 95); I^2=54%	-	-	-	0.92 (0.89 to 0.94)
Multiparametric MRI	9	40 (16 to 71); I^2=5%	92 (80 to 97); I^2=91%	-	-	-	0.82 (0.79 to 0.86)

AUC: area under the curve; DOR: diagnostic odds ratio; MRI: magnetic resonance imaging; NPV: negative predictive value; PET: positron emission tomography; PPV: positive predictive value; PSMA: prostate-specific membrane antigen.

PROSTATE CANCER MANAGEMENT

Systematic Reviews

Systematic reviews conducted by Mazrani et al (2022)[31,] and Pozdnyakov et al (2022)[32,] assessed the effect of PSMA PET imaging for detection of biochemical prostate cancer recurrence, change in management, and patient outcomes following PSMA PET. Study characteristics of the reviews are summarized in Table 11. In both reviews, ^{68}GA was the imaging agent used in the majority of studies (80% [16/20] and 88% [30/34], respectively). Only 6 studies overlapped between the 2 reviews, potentially due to Mazrani et al limiting their inclusion criteria to prospective studies and differences in study search dates. Of note, the Fendler 2019 study (N=635) discussed below in the Prospective Studies section was included in both reviews, accounting for 30% of the total population in Mazrani and 17% of the total population in Pozdnyakov. Mazrani assessed the quality of the included studies using the QUADAS-2 tool. For most studies, risk of bias was determined to be high or unclear for the patient selection domain (17/20 studies) and for the reference standard domain (17/20 studies). Study quality was assessed by Pozdnyakov using National Heart, Lung, and Blood Institute (NHLBI) criteria for observational and cohort studies. Studies were scored on a scale of 0 to 14, with higher scores reflecting a lower risk of bias. Scores for individual studies ranged from 1 to 11; the median score for the change in management studies was 8, and median score for clinical outcome studies was 9. A funnel plot analysis conducted by Pozdnyakov suggested the presence of publication bias (Egger's test p=.008).

Table 11. Characteristics of Systematic Reviews of PSMA PET Imaging for Prostate Cancer Management

Study	Dates	No. of Included Studies	Reference Standard	Participants	N (Range)	Study Design(s)
Mazrani et al 2022[31,]	Through July 1, 2021	20	Conventional imaging or histopathology	Individuals with biochemical prostate cancer recurrence • Mean PSA NR; range 0.2 to 14.9 ng/mL • Initial prostate cancer treatment NR	2110 (30-635)	Prospective
Pozdnyakov et al 2022[32,]	Through October 1, 2020	34 for change in management 27 for clinical outcomes	NR	Individuals with biochemical prostate cancer recurrence • Median PSA 7.6 ng/mL at time of diagnosis and 1.3 ng/mL at time of PET imaging • 63% had a Gleason score <7 • Initial treatment: 56% radical prostatectomy, 24% radiotherapy plus radical prostatectomy, 18% radiotherapy only • Androgen-deprivation therapy prior to PET imaging: 18%	3680 for change in management 2674 for clinical outcomes	Prospective or retrospective

NR: not reported; PET: positron emission tomography; PSA: prostate-specific antigen.

Study results are summarized in Table 12. The reviews found similar proportions of individuals with positive PSMA imaging and with a change in management based on PSMA PET imaging results. Meta-regression analysis conducted by Pozdnyakov[32,] found increasing age (p=.0003), Gleason score ≥8 (p=.016), prior treatment with androgen-deprivation therapy (p<.001), initial treatment with radical prostatectomy (p=.003), and a higher PSA at initial diagnosis and the time of PET (p=.003 for both) all associated with PSMA positive imaging. Regarding change in management, PSMA positivity was the only variable with a significant association (p=.001).

Twenty-seven studies (n=2674) included in Pozdnyakov review[32,] reported clinical outcomes following PSMA PET imaging. In this subset of studies, individuals received treatment after PSMA PET with metastasis-directed radiotherapy (61%), standard salvage radiotherapy (26%), or surgical metastasectomy (8.3%). Twenty percent also received adjunctive androgen-deprivation therapy. The median duration of follow-up was 16 months across the studies, but varied according to outcome from 11 months for complete biochemical response (9 studies), 20 months for biochemical recurrence-free survival (9 studies), and 24 months for overall survival (12 studies). Heterogeneity was 75% or higher for all outcomes. Additional analyses limited to data from individuals who underwent metastasis-directed treatment found similar results for biochemical recurrence-free survival (63.7%, 95% CI, 53.3% to 74.1%) and overall survival (96.9%, 95% CI, 95.1% to 98.8%); data on complete biochemical response were too limited in this population to pool.

Table 12. Results of Systematic Reviews of PSMA PET Imaging for Prostate Cancer Management

Study	Positive PSMA Imaging	Change in Management	Complete Biochemical Response	Biochemical Recurrence-Free Survival[a]	Overall Survival
Mazrani et al 2022[31,]					
Total N	2210	330	Not reported	Not reported	Not reported
Proportion (n/N)	66.6% (1406/2110)	42.7% (141/330)	-	-	-
95% CI	-	-	-	-	-
I^2(p)	-	-	-	-	-
Podzdynakov et al 2022[32,]					
Total N	3680	Not reported	558	1057	1684
Proportion (n/N)	68.2%	56.4%	23.3%	60.2%	98.3%
95% CI	-	48.0% to 63.9%	14.6% to 32.0%	49.1% to 71.4%	97.2% to 99.4%
I^2(p)	-	96%	86%	94%	75%

[a] PSA <0.2 ng/ml or <nadir

Prospective Studies

Prospective studies not included in one of the systematic reviews are summarized below. The exception is the Fendler 2019 study, which although included in both the Mazrani and Pozdnyakov reviews, is described separately as it is one of the largest studies published to date and was one of the studies upon which FDA approval of the Locametz ^{68}GA preparation kit was based (see Prostate Cancer Treatment, below).

Jani et al (2023) published results from the SPOTLIGHT trial, which was a prospective, open-label, multicenter, phase 3 study to assess the diagnostic performance and safety of flotufolastat-F18.[33,] Men (N=389) with elevated PSA levels suspicious for recurrent prostate cancer were

administered an intravenous bolus of flotufolastat-F^{18} 50-70 minutes before PET/CT. Three separate, blinded readers each provided their local interpretation of the images. Among the patients with an evaluable scan, the total flotufolastat-F^{18} detection rate was 83%. Verified detection rates ranged from 51% (95% CI, 46.1 to 56.6) to 54% (95% CI, 48.8 to 59.3) among the 366 patients for whom a standard of truth (histopathology [n=69]/confirmatory imaging only [n=297]) was available which surpassed the prespecified statistical threshold. The total region-level PPV fell short of the prespecified threshold, ranging from 46% (95% CI 42.0 to 50.3) to 60% (95% CI 55.1 to 65.5).

Surasi et al (2023) conducted a prospective, open-label, multicenter, phase 3 study (LIGHTHOUSE) to evaluate the diagnostic performance and safety of flotufolastat-F18 in patients with newly diagnosed prostate cancer. [34,] Men (N=356) with biopsy-proven adenocarcinoma of the prostate and unfavorable intermediate- to very-high-risk disease classification were administered an intravenous bolus of flotufolastat-F^{18} 50-70 minutes before PET/CT. Three separate, blinded readers each provided their local interpretation of the images. For readers 1, 2, and 3, the sensitivity for pelvic lymph node detection was 30% (95% CI, 19.6 to 42.1), 27% (95% CI, 17.2 to 39.1), and 23% (95% CI, 13.7 to 34.4), respectively, not reaching the predetermined threshold. Specificity exceeded the criteria for all readers with 93% (95% CI, 88. to 95.9), 94% (95% CI, 89.8 to 96.6), and 97% (95% CI, 93.7 to 98.7), respectively.

Hofman et al (2020) published results from the multicenter, randomized proPSMA trial (N=300) that evaluated the diagnostic utility of ^{68}Ga-PSMA PET/CT as a replacement for conventional imaging in newly diagnosed individuals with prostate cancer and high-risk features.[35,] Individuals were randomly assigned 1:1 to receive ^{68}Ga-PSMA PET/CT or conventional imaging prior to radical prostatectomy or radiotherapy with curative intent. The primary outcome was accuracy for identifying either pelvic nodal or distant-metastatic disease. A reference standard was assessable for 98% of individuals, with 30% of the cohort positive for nodal or distant metastases. ^{68}Ga-PSMA PET/CT had an improved sensitivity (85% vs. 38%) and specificity (98% vs. 91%) compared to conventional imaging. This translated to a greater AUC for accuracy with ^{68}Ga-PSMA PET/CT (92% vs. 65% with conventional imaging; absolute difference, 27%; 95% CI, 23 to 31, p<.0001). A change in intended management was reported more frequently with ^{68}Ga-PSMA PET/CT compared to conventional imaging (28% vs. 15%, p=.008).

Pienta et al (2021) published results from the prospective Phase 2/3, multi-center Study of 18-F-DCFPyL PET/CT imaging in individuals with prostate cancer: Examination of diagnostic accuracy (OSPREY) trial[36,]. Two different cohorts were evaluated: individuals with high-risk prostate cancer undergoing radical prostatectomy with pelvic lymphadenectomy (cohort A) and individuals with suspected recurrent/metastatic prostate cancer on conventional imaging (cohort B). Both cohorts received conventional imaging at baseline and piflufolastat-F^{18} PET/CT 4 to 6 weeks later. In cohort A, 268 individuals with high-risk prostate cancer were evaluable to determine the diagnostic performance of piflufolastat-F^{18} PET/CT in detecting pelvic nodal metastases. The median specificity was 97.9% (95% CI, 94.5% to 99.4%) and median sensitivity was 40.3% (95% CI, 28.1% to 52.5%). The sensitivity end point was not met, as the lower bounds of the 95% CI did not reach the pre-specified success threshold of 40%. In cohort B, 93 individuals were analyzed to assess the diagnostic performance for detecting sites of prostate cancer metastases or locoregional occurrence. Median sensitivity was 95.8% (95% CI, 87.8% to 99.0%) and median PPV was 81.9% (95% CI, 73.7% to 90.2%). Specificity was not reported.

Morris et al (2021) published results from the CONDOR trial, which was a prospective, multicenter, phase 3 study.[37,] The performance of piflufolastat-F^{18} PET/CT in individuals with biochemical recurrence and uninformative conventional imaging (including ^{18}F-fluciclovine or ^{11}C-choline PET, CT, MRI, and/or whole-body bone scintigraphy) was evaluated. The primary endpoint was correct localization rate, a measure of PPV plus anatomic lesion colocalization based on histopathology, imaging findings, or therapy response. It was further defined as the percentage of individuals with a 1:1 correspondence between at least 1 lesion identified on piflufolastat-F^{18} PET/CT by central readers and the composite standard of truth. The FDA considered correct localization rate to functionally represent a patient-level PPV.[38,] It also stated that due to high disease prevalence in individuals with biochemically recurrent prostate cancer, true negative regions are difficult to identify and would require long-term follow-up. Thus, specificity is not considered a practical endpoint in this patient population. However, "PPV can also provide some information related to false positive patients and is much more readily estimated."

The CONDOR trial included 208 individuals (median PSA of 0.8 ng/mL) who received piflufolastat-F^{18} PET/CT.[37,] The correct localization rate across the 3 readers ranged from 84.8% to 87.0% (lower bound of 95% CI, 77.8 to 80.4), meeting the pre-specified success threshold of 20% for the lower bound of the 95% CI in the primary analysis, which excluded individuals with a negative PET result or if there was no reference standard data available for a PET-positive region. The detection rate rose with increasing PSA levels ranging from 36.2% (<0.5 ng/mL) to 96.7% (≥5 ng/mL). A change in intended management was reported in 63.9% (131/205) of evaluable individuals.

Hope et al (2021) included 764 individuals with intermediate or high-risk prostate cancer undergoing ^{68}GA PSMA PET imaging, 277 of whom had subsequent radical prostatectomy and pelvic lymph node dissection.[39,] The median PSA was 11.4 mg/ml, and 78% of the study population was high-risk, based on D'Amico risk classification. Compared with a histopathological reference standard, sensitivity of ^{68}GA PSMA PET in this population was 40% (95% CI, 34 to 46), specificity 95% (95% CI, 92 to 97), PPV 75% (95% CI, 70 to 80), and NPV 81% (95% CI, 76 to 85).

Fendler et al (2019) conducted a prospective single-arm clinical trial to evaluate the accuracy of ^{68}Ga-PSMA PET/CT in individuals with biochemically recurrent prostate cancer after prostatectomy, radiation therapy, or both.[40,] The primary endpoint was PPV on a per-patient and per-region basis of ^{68}Ga-PSMA PET for detection of tumor location. A total of 635 individuals were enrolled. On a per-patient basis, PPV was 84% (95% CI, 75 to 90) by histopathologic validation (primary endpoint, n=87) and 92% (95% CI, 88 to 95) by the composite reference standard (n=217). Detection rates significantly increased with increasing PSA levels.

Prostate Cancer Treatment

Individuals with previously treated metastatic castration-resistant prostate cancer (mCRPC) who are potential candidates for treatment with ^{177}Lu-vipivotide tetraxetan (Pluvicto) should undergo PSMA PET imaging to appropriately select those individuals with PSMA-positive lesions. The Locametz ^{68}GA preparation kit received FDA approval as a theranostic agent in conjunction with Pluvicto, although Pluvicto labeling indicates that other PSMA PET imaging agents may also be used for identification of PSMA-positive individuals. FDA approval of Locametz was based on the Hope et al (2021)[39,] and Fendler et al (2019)[40,] studies, described above.

GUIDELINES

National Comprehensive Cancer Network

NCCN guidelines for initial workup of suspected prostate cancer (v.2.2025) recommend multiparametric MRI prior to biopsy in certain individuals and include no recommendations on the use of PSMA PET or PET/CT.[41,]

NCCN prostate cancer treatment guidelines (v.2.2026)[25,] indicate that flotufolastat-F^{18}, piflufolastat-F^{18} or ^{68}Ga-PSMA PET/CT or PET/MRI imaging may be appropriate following equivocal standard imaging or as an alternative to standard imaging for initial staging of individuals who are symptomatic and/or with a life expectancy >5 years with unfavorable intermediate-, high-, or very high-risk disease, for the detection of biochemically recurrent disease following initial definitive therapy, and as part of a workup for progression in individuals with N1 cancer on androgen deprivation therapy or localized cancer on observation. The guidelines include the following specific imaging recommendations:

- CT, MRI, or PET/CT or PET/MRI with F-18 piflufolastat PSMA, Ga-68 PSMA-11, F-18 flotufolastat PSMA, F-18 sodium fluoride, C-11 choline, or F-18 fluciclovine can be considered for equivocal results on initial bone scan.
- Bone imaging can be achieved by conventional technetium-99m-MDP bone scan.
    - Plain films, CT, MRI, or PET/CT or PET/MRI with F-18 sodium fluoride, C-11 choline, F-18 fluciclovine, Ga-68 prostate-specific membrane antigen (PSMA)-11, F-18 flotufolastat PSMA, or F-18 piflufolastat PSMA can be considered for equivocal results on initial bone imaging.

- Soft tissue imaging of the pelvis, abdomen, and chest can include chest CT and abdominal/pelvic CT or abdominal/pelvic MRI. mpMRI is preferred over CT for pelvic staging.

- Alternatively, Ga-68 PSMA-11 F-18 piflufolastat PSMA, or F-18 flotufolastat PSMA PET/CT or PET/MRI can be considered for bone and soft tissue (full body) imaging.
    - Because of the increased sensitivity and specificity of PSMA-PET tracers for detecting micrometastatic disease compared to conventional imaging (CT, MRI) at both initial staging and biochemical recurrence, the Panel does not feel that conventional imaging is a necessary prerequisite to PSMA-PET and that PSMA-PET/CT or PSMA-PET/MRI can serve as an equally effective, if not more effective front- line imaging tool for these patients.

Imaging (including PSMA PET) is not recommended for individuals with asymptomatic very low, low, or favorable intermediate risk disease and life expectancy of ≤5 years.

Society of Nuclear Medicine and Molecular Imaging

The SNMMI has published appropriate use criteria (2022) for PSMA PET imaging.[42,] Panel recommendations for PSMA PET imaging are as follows, based on clinical scenarios and appropriate use scores (scale 1-9):

- Appropriate use scenarios (score 7-9)

  - Newly diagnosed unfavorable intermediate-, high-risk, or very-high-risk prostate cancer (score: 8)
  - Newly diagnosed unfavorable intermediate-, high-risk, or very-high-risk prostate cancer with negative/equivocal or oligometastatic disease on conventional imaging (score: 8)
  - PSA persistence or PSA rise from undetectable level after radical prostatectomy (score: 9)
  - PSA rise above nadir after definitive radiotherapy (score: 9)
  - nmCRPC (M0) on conventional imaging (score: 7)

- Potentially appropriate use scenarios (score 4-6)
  - Newly diagnosed prostate cancer with widespread metastatic disease on conventional imaging (score 4)
  - PSA rise after focal therapy of the primary tumor (score 5)
  - Posttreatment PSA rise in the mCRPC setting (score 6)
  - Evaluation of response to therapy (score 5)

- Rarely appropriate use scenarios (score 1-3)
  - Patients with suspected prostate cancer (e.g., high/rising PSA levels, abnormal digital rectal examination results) evaluated for targeted biopsy and detection of intraprostatic tumor (score 3)
  - Patients with very-low, low-, and favorable intermediate-risk prostate cancer (score: 2)

American Society of Clinical Oncology
The American Society of Clinical Oncology (2021) recommends against the use of "PET, CT, and radionuclide bone scans, or newer imaging scans in the staging of early prostate cancer at low risk for metastasis."[43,] The recommendations note that current evidence does not support the use of PSMA PET imaging modalities for staging newly diagnosed prostate cancer with low risk of distant metastasis based on clinicopathologic features (grade 1 disease, T1c/T2a disease, prostate-specific antigen (PSA) <10 ng/ml, Gleason score ≤6).

American Urological Association et al
The American Urological Association (AUA)/American Society for Radiation Oncology (ASTRO; 2022)[44,] joint guideline on risk assessment, staging and risk-based management of clinically localized prostate cancer includes the following statements:

- Clinicians should not routinely perform abdomino-pelvic computed tomography (CT) scan or bone scan in asymptomatic patients with low- or intermediate-risk prostate cancer. (Expert Opinion)

- Clinicians should obtain a bone scan and either pelvic multi-parametric magnetic resonance imaging (mpMRI) or CT scan for patients with high-risk prostate cancer. (Strong Recommendation; Evidence Level: Grade B)

  - To evaluate for the presence of bone metastasis, conventional bone scan should be obtained as the initial staging study. As robust evidence to support an imaging evaluation in unfavorable intermediate-risk disease remains lacking, the Panel

offers that clinicians may consider obtaining staging imaging for patients within this risk classification.

- In patients with prostate cancer at high risk for metastatic disease with negative conventional imaging, clinicians may obtain molecular imaging to evaluate for metastases. (Expert Opinion)

The guideline notes "while data to date supporting a clinical benefit to novel imaging modalities for patients with negative conventional imaging remain quite limited, the Panel did conclude that clinicians may offer molecular imaging in patients at high risk for metastatic disease based on the demonstrated enhanced staging accuracy."

The guideline states that the systematic review used to provide evidence for the AUA/ASTRO guideline conducted literature searches through September 2021. Although the systematic review has not yet been published, the literature search end date was prior to the November 2021 publication of the Hope et al[39,] prospective study (described above), which informed the updated NCCN treatment guideline. It is unclear how inclusion of the Hope et al results would impact the AUA/ASTRO guideline recommendations.

Subsection Summary: ^{68}Ga-PSMA PET, ^{68}Ga-PSMA PET/CT, Piflufolastat-F^{18} PET, and Piflufolastat-F^{18} PET/CT, Flotufolastat-F^{18} PET, and Flotufolastat-F^{18} PET/CT for Prostate Cancer

Evidence for the use of ^{68}Ga-PSMA PET, ^{68}Ga-PSMA PET/CT, piflufolastat-F^{18} PET, piflufolastat-F^{18} PET/CT, flotufolastat-F^{18} PET, and flotufolastat-F^{18} PET/CT consists of systematic reviews and prospective, multicenter trials.

A systematic review of studies conducted in individuals with suspected prostate cancer found similar sensitivity and specificity for PSMA PET and MRI for detection of clinically significant prostate cancer, but only 3 studies of 228 individuals were included in the analysis. The evidence does not support the use of PSMA PET for initial diagnosis of prostate cancer.

Systematic reviews have found PSMA PET to have similar diagnostic accuracy across risk groups in newly diagnosed individuals, and to be similar to MRI for staging intermediate/high-risk prostate cancer. Systematic reviews of studies conducted in individuals with biochemical recurrence, found high proportions with positive PSMA PET imaging often leading to change in management. Individual prospective trials have generally found that PSMA-targeted radiotracers provide a high specificity for detecting pelvic lymph node or distant metastases in newly diagnosed individuals with high-risk disease and a clinically relevant PPV in individuals with biochemical recurrence. NCCN guidelines and SNMMI recommend the use of PSMA PET in specific clinical circumstances. The evidence supports the use of ^{68}Ga-PET, ^{68}Ga-PET/CT, piflufolastat-F^{18} PET, piflufolastat-F^{18} PET/CT, flotufolastat-F^{18} PET, and flotufolastat-F^{18} PET/CT for staging, restaging, and surveillance of prostate cancer in selected individuals.

RENAL CELL CARCINOMA

Systematic Reviews

A systematic review by Ma et al (2017) evaluated the use of FDG-PET or FDG-PET/CT for restaging renal cell carcinoma (RCC).[45,] The literature search, conducted through July 2016,

identified 15 studies, mostly retrospective, for inclusion into a meta-analysis. Pooled estimates for sensitivity and specificity were 86% (95% CI, 88% to 93%) and 88% (95% CI, 84% to 91%), respectively. Reviewers concluded that PET showed potential for identifying metastatic or recurrent lesions in individuals with RCC but that more prospective studies would be needed.

A systematic review and meta-analysis by Sadaghiani et al (2024) included 9 studies (N=152) and found that PSMA-PET/CT has a high lesion-level detection rate in RCC with a pooled estimate of 0.83 (95% CI, 0.67 to 0.92; I^2=81%) overall, 0.87 (95% CI, 0.73 to 0.95) for restaging metastatic/recurrent disease, and 0.74 (95% CI, 0.57 to 0.86) for staging/evaluation of primary RCC.[46,] In comparative data from 2 studies, PSMA-PET/CT outperformed conventional imaging modalities for metastatic clear cell RCC (detection rate, 0.92; 95% CI, 0.76 to 0.97; I^2=28% vs 0.63; 95% CI, 0.50 to 0.74; I^2=0%). Heterogeneity was high, and most studies employed retrospective study designs, which were often underpowered. The authors recommend larger prospective trials, but suggest that the pooled results support PSMA-PET/CT as a promising modality.

Guidelines
Current NCCN guidelines for kidney cancer (v.1.2026) state that "The value of PET in RCC remains to be determined. Currently, PET or PET/CT alone is not a tool that is standardly used to diagnose kidney cancer or follow for evidence of relapse after nephrectomy." However, FDG-PET has a Category 2B recommendation in the following circumstances: [47,]

- "Follow-up for Stage III, or T4 NXM0 Resected:
    - FDG-PET is useful in certain circumstances (fumarate hydratase [FH]-deficient RCC or succinate dehydrogenase complex subunit B [SDHB]-deficient RCC.

- Follow-up for Relapsed or Stage IV and Surgically Unresectable Disease:
    - FDG-PET is useful in certain circumstances (bone-predominant disease, assessment prior to metastasectomy, FH-deficient RCC or SDHB-deficient RCC."

Section Summary: Renal Cell Carcinoma
The evidence does not support the use of FDG-PET and FDG-PET/CT for the diagnosis, staging and restaging, or surveillance of RCC.

TESTICULAR CANCER

Systematic Reviews
An AHRQ technology assessment conducted by Ospina et al (2008) and studies evaluating residual masses in individuals after chemotherapy for seminoma has supported the use of PET. [48,49,]

The AHRQ systematic review conducted by Matchar et al (2004) found 1 prospective study and 4 retrospective studies that generally showed higher sensitivity and specificity for PET compared with CT.[50,] However, these studies were small in size and failed to report separate results for individuals with and without seminoma. Studies also failed to report separate results by clinical stage of the disease.

In addition, studies on PET's ability to discriminate viable tumor and necrosis or fibrosis after treatment of testicular cancer were flawed in 2 main ways. First, most studies did not compare the diagnostic accuracy of PET with other imaging modalities. Second, studies that did compare PET and CT did not state a clear threshold for a positive CT test, making study results difficult to interpret. Therefore, it is uncertain whether the use of PET leads to different patient management decisions and health outcomes compared with other imaging modalities.

Guidelines
Current NCCN guidelines for testicular cancer (v.1.2026) 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).[51,] 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 individuals.

Section Summary: Testicular Cancer
Evidence for the use of PET or PET/CT in individuals with testicular cancer consists of an AHRQ systematic review of small studies. Results showed that PET or PET/CT can be useful in evaluating residual masses following chemotherapy for seminoma. There is no evidence supporting the use of PET or PET/CT in nonseminoma individuals. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of testicular cancer.

The evidence does not support the use of FDG-PET and FDG-PET/CT for surveillance of testicular cancer.

SUPPLEMENTAL INFORMATION
The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Clinical Input From Physician Specialty Societies And Academic Medical Centers
While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process, through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

Clinical input was sought to help determine whether the use of PET imaging using either of the FDA-approved prostate-specific membrane antigen (PSMA) agents for individuals with known or suspected prostate cancer would provide a clinically meaningful improvement in net health outcome and whether the use is consistent with generally accepted medical practice. In response to requests, clinical input on the use of PSMA PET was received from 2 society-level respondents.

For individuals with suspected or diagnosed prostate cancer who are in need of staging information and receive Ga-68 PSMA-11 PET/CT or F-18 Piflufolastat-PSMA PET/CT, clinical input provides consistent support that the use of FDA-approved PSMA PET agents provides a clinically meaningful improvement in the net health outcome and is consistent with generally accepted medical practice. Respondents noted such use is consistent with NCCN guidelines and SNMMI appropriate use criteria, and the high utility of PSMA PET in these clinical scenarios. In addition, respondents stated that in the ProPSMA trial (PMID 32209449), prostate cancer staging with

PSMA PET was more accurate than conventional imaging, with fewer equivocal imaging results, lower radiation exposure to the patient, and greater treatment impact.

For individuals with suspected recurrence of prostate cancer based on elevated serum PSA level who receive Ga-68 PSMA-11 PET/CT or F-18 Piflufolastat-PSMA PET/CT, clinical input provides consistent support that the use of FDA-approved PSMA PET agents provides a clinically meaningful improvement in the net health outcome and is consistent with generally accepted medical practice. Respondents noted such use is consistent with SNMMI appropriate use criteria and that the high sensitivity of PSMA PET in localizing recurrent disease has been shown to significantly affect clinical management.

For individuals with prostate cancer and in need of workup for progression who receive Ga-68 PSMA-11 PET/CT or F-18 Piflufolastat-PSMA PET/CT, clinical input provides consistent support that the use of FDA-approved PSMA PET agents provides a clinically meaningful improvement in the net health outcome and is consistent with generally accepted medical practice. Respondents provided examples of the effective use of PSMA PET imaging in accurate diagnosis of progression and noted that use of PSMA PET imaging in this clinical context is consistent with NCCN and SNMMI guidelines.

Respondents believe there is compelling evidence supporting the use of PSMA PET imaging modalities in changing disease management for the benefit of patients, while recognizing that no single imaging method should be used for all potential clinical situations (diagnosis, staging and restaging, and surveillance) because use is dependent on a strictly defined clinical context based on FDA labeling.

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.

Current National Comprehensive Cancer Network, American College of Radiology, and other relevant U.S.-based guidelines are summarized in each section of the Rationale.

U.S. Preventive Services Task Force Recommendations
Not applicable.

Ongoing and Unpublished Clinical Trials
A search of ClinicalTrials.gov in October 2025 identified a large number of ongoing and unpublished trials that might influence this review.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

CPT/HCPCS	
78811	Positron emission tomography (PET) imaging; limited area (e.g. Chest, head/neck)
78812	Positron emission tomography (PET) imaging; skull base to mid-thigh
78813	Positron emission tomography (PET) imaging; whole body
78814	Tumor imaging, positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization; limited area (e.g. chest, head/neck)
78815	Tumor imaging, positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization; skull base to mid-thigh
78816	Tumor imaging, positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization; whole body
A9515	Choline C-11 injection, diagnostic, per study dose up to 20 millicuries
A9552	Fluorodeoxyglucose F-18 FDG, diagnostic, per study dose, up to 45 millicuries
A9588	Fluciclovine f-18, diagnostic, 1 millicurie
A9593	Gallium ga-68 psma-11, diagnostic, (ucsf), 1 millicurie
A9594	Gallium ga-68 psma-11, diagnostic, (ucla), 1 millicurie
A9595	Piflufolastat f-18, diagnostic, 1 millicurie
A9596	Gallium ga-68 gozetotide, diagnostic, (illuccix), 1 millicurie
A9597	Positron emission tomography radiopharmaceutical, diagnostic, for tumor identification, not otherwise classified
A9598	Positron emission tomography radiopharmaceutical, diagnostic, for non-tumor identification, not otherwise classified
A9608	Flotufolastat f 18, diagnostic, 1 millicurie
A9616	Gallium ga-68 gozetotide (gozellix), diagnostic, 1 millicurie
A9800	Gallium ga-68 gozetotide, diagnostic, (locametz), 1 millicurie
C9067	Gallium ga-68, dotatoc, diagnostic, 0.01 mci
G0235	PET imaging, any site not otherwise specified

REVISIONS	
Posted 01-28-2025	Oncologic Applications Genitourinary was originally part of the Positron Emission Tomography (PET) Scanning: Oncologic Applications medical policy. Oncologic

REVISIONS	
Effective 02-27-2025	Applications for Genitourinary has been pulled out and placed into a separate medical policy, Positron Emission Tomography (PET) Scanning: Oncologic Applications (Genitourinary). The medical policy language was unchanged.
10-01-2025	Updated Coding Section ▪ Added new code A9616 (eff. 10-01-2025)
01-13-2026	Updated Description Section
	Updated Policy Section: ▪ Changed A1, B1, C2, D1, E1: From PET to FDG-PET/CT
	▪ Updated Policy Guidelines Section: ▪ Removed B: 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 individuals 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. ▪ 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 an individual 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 an individual with colorectal cancer is being performed to detect hepatic disease or evaluate local recurrence. Due to the complicated hierarchy of imaging options in individuals with malignancy and complex 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 individuals at various intervals. This is not the same as the use of PET for detecting recurrent disease in symptomatic individuals; these applications of PET are considered within tumor-specific categories in the policy statements.
	Updated Rationale Section
	Updated Reference Section

REFERENCES

1. Riberich R. FDA-Approved PET Radiopharmaceuticals. http://www.radiopharmaceuticals.info/pet-radiopharmaceuticals.html. Accessed October 20, 2025.
2. Jadvar H. Prostate-specific Membrane Antigen PET: Standard Imaging in Prostate Cancer. Radiology. Sep 2022; 304(3): 609-610. PMID 35608452
3. Abdlkadir AS, Al-Adhami D, Allouzi S, et al. Diagnostic efficacy of [18 F]FDG PET/CT and [18 F]FDG PET/MRI in preoperative staging of locoregional urinary bladder cancer: a systematic review and Meta-Analysis. Discov Oncol. Jul 01 2025; 16(1): 1241. PMID 40591083

4. van der Pol CB, Sahni VA, Eberhardt SC, et al. ACR Appropriateness Criteria ® Pretreatment Staging of Muscle-Invasive Bladder Cancer. J Am Coll Radiol. May 2018; 15(5S): S150-S159. PMID 29724418
5. Allen BC, Oto A, Akin O, et al. ACR Appropriateness Criteria® Post-Treatment Surveillance of Bladder Cancer: 2021 Update. J Am Coll Radiol. May 2021; 18(5S): S126-S138. PMID 33958107
6. Lee SW, Kim SJ. Diagnostic Performance of 18F-FDG PET/CT for Lymph Node Staging in Penile Cancer. Clin Nucl Med. May 01 2022; 47(5): 402-408. PMID 35143458
7. Jakobsen JK, Frahm Nielsen T, Ipsen P, et al. DaPeCa-7: comparative assessment of fluorodeoxyglucose positron emission tomography/computed tomography (CT) and conventional diagnostic CT in diagnosis of lymph node metastases, distant metastases and incidental findings in patients with invasive penile cancer. BJU Int. Feb 2021; 127(2): 254-262. PMID 33448605
8. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Penile Cancer. Version 2.2025. https://www.nccn.org/professionals/physician_gls/pdf/penile.pdf. Accessed October 18, 2025.
9. Liu J, Chen Z, Wang T, et al. Influence of Four Radiotracers in PET/CT on Diagnostic Accuracy for Prostate Cancer: A Bivariate Random-Effects Meta-Analysis. Cell Physiol Biochem. 2016; 39(2): 467-80. PMID 27383216
10. Ouyang Q, Duan Z, Lei J, et al. Comparison of meta-analyses among elastosonography (ES) and positron emission tomography/computed tomography (PET/CT) imaging techniques in the application of prostate cancer diagnosis. Tumour Biol. Mar 2016; 37(3): 2999-3007. PMID 26415734
11. Biscontini G, Romagnolo C, Cottignoli C, et al. 18F-Fluciclovine Positron Emission Tomography in Prostate Cancer: A Systematic Review and Diagnostic Meta-Analysis. Diagnostics (Basel). Feb 13 2021; 11(2). PMID 33668673
12. Fanti S, Minozzi S, Castellucci P, et al. PET/CT with (11)C-choline for evaluation of prostate cancer patients with biochemical recurrence: meta-analysis and critical review of available data. Eur J Nucl Med Mol Imaging. Jan 2016; 43(1): 55-69. PMID 26450693
13. von Eyben FE, Kairemo K. Meta-analysis of (11)C-choline and (18)F-choline PET/CT for management of patients with prostate cancer. Nucl Med Commun. Mar 2014; 35(3): 221-30. PMID 24240194
14. Umbehr MH, Müntener M, Hany T, et al. The role of 11C-choline and 18F-fluorocholine positron emission tomography (PET) and PET/CT in prostate cancer: a systematic review and meta-analysis. Eur Urol. Jul 2013; 64(1): 106-17. PMID 23628493
15. Mohsen B, Giorgio T, Rasoul ZS, et al. Application of C-11-acetate positron-emission tomography (PET) imaging in prostate cancer: systematic review and meta-analysis of the literature. BJU Int. Dec 2013; 112(8): 1062-72. PMID 23937453
16. Sandgren K, Westerlinck P, Jonsson JH, et al. Imaging for the Detection of Locoregional Recurrences in Biochemical Progression After Radical Prostatectomy-A Systematic Review. Eur Urol Focus. Jul 2019; 5(4): 550-560. PMID 29133278
17. Albisinni S, Aoun F, Marcelis Q, et al. Innovations in imaging modalities for recurrent and metastatic prostate cancer: a systematic review. Minerva Urol Nefrol. Aug 2018; 70(4): 347-360. PMID 29388415
18. Jani AB, Schreibmann E, Goyal S, et al. 18 F-fluciclovine-PET/CT imaging versus conventional imaging alone to guide postprostatectomy salvage radiotherapy for prostate

cancer (EMPIRE-1): a single centre, open-label, phase 2/3 randomised controlled trial. Lancet. May 22 2021; 397(10288): 1895-1904. PMID 33971152
19. Dreyfuss AD, Ahn GS, Barsky AR, et al. 18F-Fluciclovine PET/CT in Therapeutic Decision Making for Prostate Cancer: A Large Single-Center Practice-Based Analysis. Clin Nucl Med. Mar 01 2021; 46(3): 187-194. PMID 33315672
20. Andriole GL, Kostakoglu L, Chau A, et al. The Impact of Positron Emission Tomography with 18F-Fluciclovine on the Treatment of Biochemical Recurrence of Prostate Cancer: Results from the LOCATE Trial. J Urol. Feb 2019; 201(2): 322-331. PMID 30179618
21. Akin-Akintayo OO, Jani AB, Odewole O, et al. Change in Salvage Radiotherapy Management Based on Guidance With FACBC (Fluciclovine) PET/CT in Postprostatectomy Recurrent Prostate Cancer. Clin Nucl Med. Jan 2017; 42(1): e22-e28. PMID 27749412
22. Treglia G, Ceriani L, Sadeghi R, et al. Relationship between prostate-specific antigen kinetics and detection rate of radiolabelled choline PET/CT in restaging prostate cancer patients: a meta-analysis. Clin Chem Lab Med. May 2014; 52(5): 725-33. PMID 24310773
23. Froemming AT, Verma S, Eberhardt SC, et al. ACR Appropriateness Criteria ® Post-treatment Follow-up Prostate Cancer. J Am Coll Radiol. May 2018; 15(5S): S132-S149. PMID 29724417
24. Lowrance WT, Breau RH, Chou R, et al. Advanced Prostate Cancer: AUA/ASTRO/SUO Guideline PART I. J Urol. Jan 2021; 205(1): 14-21. PMID 32960679
25. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer. Version 2.2026. https://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed October 17, 2025.
26. Jadvar H, Ballas LK, Choyke PL, et al. Appropriate Use Criteria for Imaging Evaluation of Biochemical Recurrence of Prostate Cancer After Definitive Primary Treatment. Journal of Nuclear Medicine. Apr 1 2020; 61(4): 552-562.
27. Eissa A, Elsherbiny A, Coelho RF, et al. The role of 68Ga-PSMA PET/CT scan in biochemical recurrence after primary treatment for prostate cancer: a systematic review of the literature. Minerva Urol Nefrol. Oct 2018; 70(5): 462-478. PMID 29664244
28. Kawada T, Yanagisawa T, Rajwa P, et al. Diagnostic Performance of Prostate-specific Membrane Antigen Positron Emission Tomography-targeted biopsy for Detection of Clinically Significant Prostate Cancer: A Systematic Review and Meta-analysis. Eur Urol Oncol. Aug 2022; 5(4): 390-400. PMID 35715320
29. Stabile A, Pellegrino A, Mazzone E, et al. Can Negative Prostate-specific Membrane Antigen Positron Emission Tomography/Computed Tomography Avoid the Need for Pelvic Lymph Node Dissection in Newly Diagnosed Prostate Cancer Patients? A Systematic Review and Meta-analysis with Backup Histology as Reference Standard. Eur Urol Oncol. Feb 2022; 5(1): 1-17. PMID 34538770
30. Wang X, Wen Q, Zhang H, et al. Head-to-Head Comparison of 68 Ga-PSMA-11 PET/CT and Multiparametric MRI for Pelvic Lymph Node Staging Prior to Radical Prostatectomy in Patients With Intermediate to High-Risk Prostate Cancer: A Meta-Analysis. Front Oncol. 2021; 11: 737989. PMID 34745959
31. Mazrani W, Cook GJR, Bomanji J. Role of 68Ga and 18F PSMA PET/CT and PET/MRI in biochemical recurrence of prostate cancer: a systematic review of prospective studies. Nucl Med Commun. Jun 01 2022; 43(6): 631-637. PMID 35438666
32. Pozdnyakov A, Kulanthaivelu R, Bauman G, et al. The impact of PSMA PET on the treatment and outcomes of men with biochemical recurrence of prostate cancer: a

systematic review and meta-analysis. Prostate Cancer Prostatic Dis. Jun 2023; 26(2): 240-248. PMID 35440642
33. Jani AB, Ravizzini GC, Gartrell BA, et al. Diagnostic Performance and Safety of 18 F-rhPSMA-7.3 Positron Emission Tomography in Men With Suspected Prostate Cancer Recurrence: Results From a Phase 3, Prospective, Multicenter Study (SPOTLIGHT). J Urol. Aug 2023; 210(2): 299-311. PMID 37126069
34. Surasi DS, Eiber M, Maurer T, et al. Diagnostic Performance and Safety of Positron Emission Tomography with 18 F-rhPSMA-7.3 in Patients with Newly Diagnosed Unfavourable Intermediate- to Very-high-risk Prostate Cancer: Results from a Phase 3, Prospective, Multicentre Study (LIGHTHOUSE). Eur Urol. Oct 2023; 84(4): 361-370. PMID 37414702
35. Hofman MS, Lawrentschuk N, Francis RJ, et al. Prostate-specific membrane antigen PET-CT in patients with high-risk prostate cancer before curative-intent surgery or radiotherapy (proPSMA): a prospective, randomised, multicentre study. Lancet. Apr 11 2020; 395(10231): 1208-1216. PMID 32209449
36. Pienta KJ, Gorin MA, Rowe SP, et al. A Phase 2/3 Prospective Multicenter Study of the Diagnostic Accuracy of Prostate Specific Membrane Antigen PET/CT with 18 F-DCFPyL in Prostate Cancer Patients (OSPREY). J Urol. Jul 2021; 206(1): 52-61. PMID 33634707
37. Morris MJ, Rowe SP, Gorin MA, et al. Diagnostic Performance of 18 F-DCFPyL-PET/CT in Men with Biochemically Recurrent Prostate Cancer: Results from the CONDOR Phase III, Multicenter Study. Clin Cancer Res. Jul 01 2021; 27(13): 3674-3682. PMID 33622706
38. Food and Drug Administration. Piflufolastat F 18 (PYLARIFY): Multi-disciplinary Review and Evaluation. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2021/214793Orig1s000MultidisciplineR.pdf Accessed October 20, 2025.
39. Hope TA, Eiber M, Armstrong WR, et al. Diagnostic Accuracy of 68Ga-PSMA-11 PET for Pelvic Nodal Metastasis Detection Prior to Radical Prostatectomy and Pelvic Lymph Node Dissection: A Multicenter Prospective Phase 3 Imaging Trial. JAMA Oncol. Nov 01 2021; 7(11): 1635-1642. PMID 34529005
40. Fendler WP, Calais J, Eiber M, et al. Assessment of 68Ga-PSMA-11 PET Accuracy in Localizing Recurrent Prostate Cancer: A Prospective Single-Arm Clinical Trial. JAMA Oncol. Jun 01 2019; 5(6): 856-863. PMID 30920593
41. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Prostate Cancer Early Detection. Version 2.2025. https://www.nccn.org/professionals/physician_gls/pdf/prostate_detection.pdf. Accessed October 16, 2025.
42. Jadvar H, Calais J, Fanti S, et al. Appropriate Use Criteria for Prostate-Specific Membrane Antigen PET Imaging. J Nucl Med. Jan 2022; 63(1): 59-68. PMID 34593595
43. American Society of Clinical Oncology. Choosing Wisely: Ten Things Physicians and Patients Should Questions. Accessed October 20, 2025.
44. Eastham JA, Auffenberg GB, Barocas DA, et al. Clinically Localized Prostate Cancer: AUA/ASTRO Guideline, Part I: Introduction, Risk Assessment, Staging, and Risk-Based Management. J Urol. Jul 2022; 208(1): 10-18. PMID 35536144
45. Ma H, Shen G, Liu B, et al. Diagnostic performance of 18F-FDG PET or PET/CT in restaging renal cell carcinoma: a systematic review and meta-analysis. Nucl Med Commun. Feb 2017; 38(2): 156-163. PMID 27824726

46. Sadaghiani MS, Baskaran S, Gorin MA, et al. Utility of PSMA PET/CT in Staging and Restaging of Renal Cell Carcinoma: A Systematic Review and Metaanalysis. J Nucl Med. Jul 01 2024; 65(7): 1007-1012. PMID 38782453
47. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Kidney Cancer. Version 1.2026. https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf. Accessed October 19, 2025.
48. Ospina MB, Horton J, Seida J, et al. Technology Assessment Report : Positron emission tomography for nine cancers (bladder, brain, cervical, kidney, ovarian, pancreatic, prostate, small cell lung, testicular). Rockville, MD: Agency for Healthcare Research and Quality; 2008.
49. Becherer A, De Santis M, Karanikas G, et al. FDG PET is superior to CT in the prediction of viable tumour in post-chemotherapy seminoma residuals. Eur J Radiol. May 2005; 54(2): 284-8. PMID 15837411
50. Matchar DB, Kulasingam SL, Havrilesky L, et al. Positron Emission Testing for Six Cancers (Brain, Cervical, Small Cell Lung, Ovarian, Pancreatic and Testicular). Rockville, MD: Agency for Healthcare Research and Quality; 2004.
51. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Testicular Cancer. Version 1.2026. https://www.nccn.org/professionals/physician_gls/pdf/testicular.pdf. Accessed October 15, 2025.
52. Centers for Medicare & Medicaid Services (CMS). Pub 100-03 National Coverage Determination (NCD) for Positron Emission TOMOGRAPHY (FDG) for Oncologic Conditions (220.6.17), https://tinyurl.com/7hc7hvpr. Accessed October 20, 2025.

OTHER REFERENCES

1. MCMC, Medical Care Ombudsman Program (MCOP), August 11, 2006, MCOP ID 1071-0720.
2. Considine oncology consultant (#372), January 23, 2007, Reference: Semin Nucl Med. 2006 Jan;36(1):93-104. Links Positron emission tomography in gynecologic cancer. Yen TC, Lai CH.
3. Blue Cross and Blue Shield of Kansas, Oncology Liaison Committee meeting, February 2003, February 2004, June 2022, July 2023, July 2025.
4. Blue Cross and Blue Shield of Kansas, Radiology Liaison Committee meeting, February 2002, February 2003. February 2009, January 2018, May 2019.
5. Blue Cross and Blue Shield of Kansas Urology Liaison Committee August 2018, June 2020, June 2025.