BlueCross BlueShield Federal Employee Program.

FEP Medical Policy Manual

FEP 6.01.26 Oncologic Applications of Positron Emission Tomography Scanning (Genitourinary)

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Related Policies:

5.21.191- Pluvicto
6.01.06 - Miscellaneous (Noncardiac, Nononcologic) Applications of Fluorine 18 Fluorodeoxyglucose Positron Emission Tomography
6.01.20 - Cardiac Applications of Positron Emission Tomography Scanning
6.01.51 - Interim Positron Emission Tomography Scanning in Oncology to Detect Early Response During Treatment
6.01.61 - Oncologic Applications of Positron Emission Tomography Scanning (Gastrointestinal and Pancreatic)
6.01.62 - Oncologic Applications of Positron Emission Tomography Scanning (Breast and Gynecologic)
6.01.63 - Oncologic Applications of Positron Emission Tomography Scanning (Bone Sarcoma and Soft Tissue Sarcoma)
6.01.64 - Oncologic Applications of Positron Emission Tomography Scanning (Hematologic)
6.01.65 - Oncologic Applications of Positron Emission Tomography Scanning (Lung)
6.01.66 - Oncologic Applications of Positron Emission Tomography Scanning (Thyroid, Neuroendocrine, Head and Neck)
6.01.67 - Oncologic Applications of Positron Emission Tomography Scanning (Brain, Melanoma, Unknown Primary)

Oncologic Applications of Positron Emission Tomography Scanning (Genitourinary)

Description

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.

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 genitorurinary cancers.

POLICY STATEMENT

Bladder Cancer

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.

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

Penile Cancer

FDG-PET/CT scanning may be considered **medically necessary** for staging and restaging in individuals with suspected inguinal lymph node positive disease.

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

Prostate Cancer

PET scanning with C 11 (carbon) choline and fluorine 18 fluciclovine may be considered **medically necessary** for evaluating equivocal initial bone scan results or f detect small volume disease in soft tissues or bone.

PET/CT or PET/MRI scanning with gallium 68-prostate-specific membrane antigen (PSMA), flotufolastat fluorine-18, and piflufolastat fluorine-18 may be considered **medically necessary** for any of the following applications:

- Individuals with diagnosed prostate cancer in need of staging information and:
    - NCCN unfavorable intermediate-, high-, or very-high-risk prostate cancer (see Policy Guidelines); OR
    - NCCN unfavorable intermediate-, high-, or very-high-risk prostate cancer with equivocal results or oligometastatic disease on initial conventional imaging (see Policy Guidelines).
- Individuals with suspected recurrence of prostate cancer based on serum PSA level who have received:
    - Radical prostatectomy with PSA level persistence or rise from undetectable level (see Policy Guidelines); OR
    - Definitive radiotherapy with PSA rise above nadir (see Policy Guidelines).
- Individuals with treated prostate cancer (including active surveillance/observation) in need of imaging as part of a workup for progression (see Policy Guidelines).
- Individuals with metastatic prostate cancer for whom lutetium Lu-177 vipivotide tetraxetan PSMA-directed therapy is indicated.

Use of gallium 68-prostate-specific membrane antigen, flotufolastat fluorine-18, and piflufolastat fluorine-18 in known or suspected prostate cancer is considered **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.

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

Renal Cell Carcinoma

FDG-PET or FDG-PET/CT scanning is considered **investigational** in all aspects of diagnosis and management of renal cancer.

Testicular Cancer

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).

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

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

Cancer Surveillance

PET scanning is considered **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

Selection Criteria

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.

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.

FDG-PET/CT is not recommended to be used routinely for staging prostate cancer.

FDG-PET/CT is not recommended for the evaluation or management of nonseminoma testicular cancer.

BENEFIT APPLICATION

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

FDA 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
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.

RATIONALE

Summary of Evidence

Bladder Cancer

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

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

Penile Cancer

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

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

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

Prostate Cancer

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

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

For individuals who have suspected prostate cancer who receive ^{68}Ga-prostate-specific membrane antigen (PSMA) PET, ^{68}Ga-PSMA PET/CT, piflufolastat-F^{18} PET, piflufolastat-F^{18} PET/CT, flotufolastat-F^{18} PET, or flotufolastat-F^{18} PET/CT, the evidence includes a systematic review. Relevant outcome is test validity. The systematic review found similar diagnostic accuracy for PSMA PET and MRI for detection of clinically significant prostate cancer, but evidence was too limited to draw conclusions as only 3 studies of 228 individuals were included in the analysis. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who have diagnosed prostate cancer and in need of staging or restaging information who receive ^{68}Ga-prostate-specific membrane antigen (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**,** the evidence includes systematic reviews and prospective, multicenter trials. Relevant outcome is test validity. Systematic reviews have found PSMA PET to have similar diagnostic accuracy across prostate cancer 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 PET provides 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. The evidence is sufficient to determine that the technology results in an improvement in the net health outcome.

For individuals who are asymptomatic after completing prostate cancer treatment who receive ^{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**,** there is no evidence on clinical outcomes. Relevant outcome that has been studied is test validity. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Renal Cell Carcinoma

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

Testicular Cancer

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

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

SUPPLEMENTAL INFORMATION

Practice Guidelines and Position Statements

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

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.

Medicare National Coverage

The Medicare coverage policy on positron emission tomography scans, which was updated in 2013, is summarized in Appendix Table 5.[52,]

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, Mntener 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.

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

Date	Action	Description
June 2012	New policy	
June 2013	Replace policy	Policy updated with literature review. References 22-35 added, Policy statements revised with NMN added to breast cancer, colorectal cancer, soft tissue sarcomas and thyroid cancer. Thyroid cancer revised to include both differentiated and poorly differentiated disease, Prostate cancer moved to section on Other Oncologic Applications, also added to this section, are diagnosis of brain tumors, restaging of gastric cancer, staging of multiple myeloma, evaluation of neuroendocrine tumors and staging of inguinal lymph nodes in patients with squamous cell carcinoma of the penis.
June 2014	Replace policy	Policy was revised with literature search adding references 37-40, 42-75. PET for gastric cancer as medically necessary for initial work up and staging and for evaluation of recurrent gastric cancer when other imaging modalities are inconclusive.
June 2015	Replace policy	Policy revised with literature review; references 1, 42-43, 46, 48-50, 58, 62, 72, 77, 84, and 87 added. Policy statements unchanged.
September 2017	Replace policy	Policy revised with literature review through March 23, 2017; references 37,41, 48-50, 59-63, 67, 69-70, 73, 76-80, 85, 94-98, 103, 109-110, 112, 115,119-120, and 126 added. Additional details added to policy statements. The following statements were changed to medically necessary: staging or restaging of brain cancer; evaluation of response to treatment in head and neck cancer; and testing with 11C-choline for evaluating response to primary treatment in prostate cancer. Two additional indications were added
December 2019	Replace policy	Policy revised with literature review through August 9, 2019; references on NCCN updated. Policy statements unchanged
December 2020	Replace policy	Policy revised with literature review through July 15, 2020; references added. Policy statements unchanged.
December 2021	Replace policy	Policy revised with literature review through August 5, 2021; references added. PET scanning for patients with suspected inguinal lymph node positive disease was added as medically necessary for staging patients. The following statements were revised to include newly approved radiotracers: "PET scanning with gallium 68 and copper 64 may be considered medically necessary as a technique for staging neuroendocrine tumors either during initial staging or for restaging at follow-up" and "PET scanning with gallium 68-prostate-specific membrane antigen and piflufolastat fluorine-18 is considered investigational in all aspects of managing prostate cancer."
June 2022	Replace policy	Prostate Cancer policy statement revised: "PET scanning with gallium 68-prostate-specific membrane antigen (Locametz) or another FDA approved PSMA-11 imaging agent specifically to select mCRPC patients for use of a targeted radioligand therapeutic agent (Pluvicto) is medically necessary
December 2022	Replace policy	Policy revised with literature review through July 12, 2022; references added. Clinical input incorporated on the use of PSMA PET imaging. The following policy statement was changed: "PET scanning with gallium 68-prostate-specific membrane antigen and piflufolastat fluorine-18 is considered medically necessary for any of the following applications: -Individuals with diagnosed prostate cancer in need of staging information and: NCCN unfavorable intermediate-, high-, or very-high-risk prostate cancer in need of staging information (see Policy Guidelines); OR NCCN unfavorable intermediate-, high-, or very-high-risk prostate cancer with equivocal results or oligometastatic disease on initial conventional imaging in need of staging information (see Policy Guidelines). -Individuals with suspected recurrence of prostate cancer based on serum PSA level who have received: radical prostatectomy with PSA level persistence or rise from undetectable level (see Policy Guidelines); OR definitive radiotherapy with PSA rise above nadir (see Policy Guidelines). -Individuals with treated prostate cancer (including active surveillance/observation) in need of imaging as part of a workup for progression (see Policy Guidelines). -Individuals with metastatic prostate cancer for whom lutetium Lu 177 vipivotide tetraxetan PSMA-directed therapy is indicated. And the following policy statement was added: "Use of gallium 68-prostate-specific membrane antigen and piflufolastat fluorine-18 in known or suspected prostate cancer is considered investigational for all other indications, including initial diagnosis and evaluation of response to therapy."

Date	Action	Description
March 2024	Replace policy	Policy updated with literature review through October 13, 2023; no references added. Extensively pruned policy by removing indications other than genitourinary cancers. Other indications moved to new policies 6.01.61, 6.01.62, 6.01.63, 6.01.64, 6.01.65, 6.01.66. and 6.01.67. Policy statements on genitorinary cancers unchanged.
December 2024	Replace policy	Policy updated with literature review through July 26, 2024; references added; guidelines updated. Medically necessary policy statements on prostate cancer modified to include new agent (flotufolastat-F18).
March 2026	Replace policy	Policy updated with literature review through October 20, 2025; references added. Editorial revision throughout policy related to use of guidelines. Intent of policy statements unchanged.