Medical Policy

BlueCross BlueShield Kansas
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Title: Positron Emission Tomography (PET) Scanning: Oncologic Applications (Breast and Gynecologic)

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
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Populations	Interventions	Comparators	Outcomes
Individuals: ▪ With diagnosed breast cancer and inconclusive results from other imaging techniques	Interventions of interest are: ▪ Adjunctive ^{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 or diagnosed breast 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 breast 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 diagnosed cervical cancer and in need of staging or restaging information	Interventions of interest are: ▪ 18F-FDG-PET or 18F-FDG-PET/CT	Comparators of interest are: ▪ Conventional imaging techniques	Relevant outcomes include: Test validity
Individuals: ▪ With suspected cervical cancer or who are asymptomatic after completing cervical 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 diagnosed endometrial cancer 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: ▪ Who are asymptomatic after completing endometrial 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
Individuals: ▪ With diagnosed ovarian 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

Populations	Interventions	Comparators	Outcomes
Individuals: ▪ With suspected ovarian cancer or who are asymptomatic after completing ovarian 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 recurrent or metastatic breast cancer to assess estrogen receptor status for treatment decisions	Interventions of interest are: • Adjunctive ^{18}F-FES-PET	Comparators of interest are: • Conventional imaging techniques • Biopsy • Immunohistochemical assay	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.

OBJECTIVE

The objective of this evidence review is to examine whether the use of PET for diagnosis, staging and restaging, and/or surveillance improves the net health outcome in individuals with breast or gynecologic 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.

Fluoroestradiol F18 (FES) is another radiotracer used in oncology imaging. FES specifically targets and binds to the estrogen receptor (ER) and its uptake, measured by PET, in breast cancer tumors is directly proportional to tumor ER expression.

REGULATORY STATUS

As of October 2025 , the following radiopharmaceuticals have been granted approval by the U.S. Food and Drug Administration, to be used with PET for breast and gynecologic cancer-related indications (see Table 1).[1,]

Cerianna™ is indicated for use with PET for the detection of estrogen receptor (ER)-positive lesions as an adjunct to biopsy in individuals with recurrent or metastatic breast cancer. Its

limitation of use states that "tissue biopsy should be used to confirm recurrence of breast cancer and to verify ER status by pathology."

Table 1. Radiopharmaceuticals Approved for Use With PET for Breast and Gynecologic Cancer Applications

Radiopharmaceutical	Manufacturer	Name	Carcinoma-Related Indication With PET
Fluorine-18 fluorodeoxyglucose (FDG)	Various		Suspected or existing diagnosis of cancer, all types
Fluorine-18 fluoroestradiol (FES)	Zionexa USA	Cerianna™	Detection of ER-positive lesions as an adjunct to biopsy in individuals with recurrent or metastatic breast cancer

ER: estrogen receptor.

POLICY

A. **Breast Cancer**
1. PET scanning using ^{18}F-FDG isotope may be considered **medically necessary** in the staging or restaging of breast cancer for the following application:
    a. Detecting locoregional or distant recurrence or metastasis (except axillary lymph nodes) when suspicion of disease is high and other imaging is inconclusive.
2. PET scanning using ^{18}F-FDG isotope is considered **experimental / investigational** in the evaluation of breast cancer for all other applications, including but not limited to the following:
    a. Differential diagnosis in individuals with suspicious breast lesions or an indeterminate or low suspicion finding on mammography.
    b. Staging axillary lymph nodes.
    c. Predicting pathologic response to neoadjuvant therapy for locally advanced disease.
3. PET scanning using fluoroestradiol F18 (FES) is considered **experimental / investigational** in individuals with breast cancer (see Policy Guidelines for exceptions).

B. **Cervical Cancer**
1. PET scanning using ^{18}F-FDG isotope may be considered **medically necessary** in the initial staging of individuals with locally advanced cervical cancer.
2. PET scanning using ^{18}F-FDG isotope may be considered **medically necessary** in the evaluation of known or suspected recurrence.

C. **Endometrial Cancer**
1. PET scanning using ^{18}F-FDG isotope is considered **medically necessary** in the:
    a. Detection of lymph node metastases, and
    b. Assessment of endometrial cancer recurrence.

D. **Ovarian Cancer**
1. PET scanning using ^{18}F-FDG isotope may be considered **medically necessary** in the evaluation of individuals with signs and/or symptoms of suspected ovarian cancer recurrence (restaging) when standard imaging, including CT scan, is inconclusive.
2. PET scanning using ^{18}F-FDG isotope is considered **experimental / investigational** in the initial evaluation of known or suspected ovarian cancer in all situations.

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.

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 15, 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 breast or gynecologic cancer.
- Individuals diagnosed with breast or gynecologic cancer and need information on the extent of cancer (initial staging upon diagnosis confirmation or restaging following treatment).
- Individuals with breast or gynecologic 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). ^{18}F fluoroestradiol (FES) is also used under certain clinical scenarios, such as determining ER status in recurrent or metastatic lesions as an adjunct to biopsy, to assess ER status in difficult to biopsy, or to evaluate extent of ER expression in indolent tumors. 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.

Clinical validity can be measured as soon as results from PET or PET/CT can be compared with results from conventional imaging techniques. Outcomes for clinical utility are long-term, which,

depending on the type of cancer, can range from months or a few years for more aggressive cancers to many years for less aggressive cancers.

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

BREAST CANCER

BREAST CANCER DIAGNOSIS

Systematic Reviews

Liang et al (2017) conducted a meta-analysis on the use of PET/CT to assess axillary lymph node metastasis.[2,] Results from the meta-analyses of 14 studies using MRI and 10 studies using PET/CT showed that MRI had a higher sensitivity in diagnosing axillary lymph node status.

In a meta-analysis of 8 studies (N=873) on FDG-PET performed in women with newly discovered suspicious breast lesions, Caldarella et al (2014) reported pooled sensitivity and specificity of 85% (95% CI, 83% to 88%) and 79% (95% CI, 74% to 83%), respectively, on a per lesion basis.[3,] As previously noted, a false-negative rate of 15% (100% - sensitivity) may be considered unacceptable given the relative ease of breast biopsy.

A systematic review by Sloka et al (2007) on PET for staging axillary lymph nodes identified 20 studies.[4,] Three of these 20 studies were rated high quality, indicating broad generalizability to a variety of individuals and no significant flaws in research methods. The remaining studies were less generalizable due to flaws in the methodology. Reviewers observed that there was great variability in estimates of sensitivity and specificity from the selected studies and that it was difficult to draw conclusions from the evidence.

Breast Cancer Staging

Zamanian et al (2023) conducted a meta-analysis of 11 studies (N=753) and reported that the sensitivity and specificity of FDG-PET/CT were greater than bone scintigraphy for detecting bone metastasis in breast cancer individuals.[5,] The sensitivity and specificity of FDG-PET/CT were 92% (95% CI, 88% to 95%) and 99% (95% CI, 96% to 100%) compared with 90% (95% CI, 86% to 93%) and 91% (95% CI, 87% to 94%) for bone scintigraphy, all respectively.

A meta-analysis by Han et al (2021) evaluated the impact of FDG- PET, PET/CT, and PET/MRI on staging and management during the initial staging of breast cancer.[6,] A total of 29 studies (N=4276) were identified. The pooled results for all 3 imaging studies demonstrated that they led to a change in staging in 25% (95% CI, 21% to 30%) of individuals and a change in management in 18% (95% CI, 14% to 23%) of individuals.

A meta-analysis by Hong et al (2013) reported a sensitivity and a specificity of FDG-PET/CT in diagnosing distant metastases in breast cancer individuals of 96% (95% CI, 90% to 98%) and 95% (95% CI, 92% to 97%), respectively, based on 8 studies (N=748).[7,] In a meta-analysis of 6 comparative studies (n=664 individuals), the sensitivity and specificity were 97% (95% CI, 84% to 99%) and 95% (95% CI, 93% to 97%) with FDG-PET/CT compared with 56% (95% CI, 38% to 74%) and 91% (95% CI, 78% to 97%) with conventional imaging, all respectively.

Rong et al (2013) conducted a meta-analysis of 7 studies (N=668 individuals) and reported that the sensitivity and specificity of FDG-PET/CT were greater than bone scintigraphy for detecting bone metastasis in breast cancer individuals.[8,] The sensitivity and specificity of FDG-PET/CT were 93% (95% CI, 82% to 98%) and 99% (95% CI, 95% to 100%) compared with 81% (95% CI, 58% to 93%) and 96% (95% CI, 76% to 100%) for bone scintigraphy, all respectively.

A meta-analysis by Isasi et al (2005) focused on PET for detecting recurrence and metastases.[9,] The analysis concluded that PET is a valuable tool; however, they did not compare PET performance with that of other diagnostic modalities, so it is unclear whether the use of PET resulted in different management decisions and health outcomes.

Breast Cancer Restaging

A systematic review by Xiao et al (2016) evaluated the diagnostic efficacy of FDG-PET and FDG-PET/CT in detecting breast cancer recurrence.[10,] The literature search, conducted through January 2016, identified 26 studies (N=1752) for inclusion in the analysis; 12 studies used PET and 14 studies used PET/CT. Fourteen studies had QUADAS scores greater than 10. Reasons for suspected recurrence in the 1752 individuals were: elevated tumor markers (57%), suspicion from conventional imaging modalities (34%), and suggestive clinical symptoms or physical examination results (9%). Pooled sensitivity and specificity are presented in Table 2. Subgroup analyses showed that PET/CT was more specific than PET alone in diagnosing recurrent breast cancer (p=.035).

A systematic review by Liu et al (2016) compared FDG-PET or FDG-PET/CT with MRI in assessing pathologic complete response to neoadjuvant chemotherapy in individuals with breast cancer.[11,] The literature search, conducted through August 2015, identified 6 studies (N=382) for inclusion. Quality assessment of the studies was deemed satisfactory using the QUADAS-2 scale. Meta-analysis results are presented in Table 2.

In another meta-analysis comparing FDG-PET with MRI and evaluating pathologic complete response to neoadjuvant chemotherapy in individuals with breast cancer, Sheikhbahaei et al (2016) selected 10 studies for analysis.[12,] The inclusion criteria differed slightly from Liu et al (2016). Liu et al (2016) required that both FDG-PET and MRI be performed before and during (or after) neoadjuvant chemotherapy, while Sheikhbahaei et al (2016) did not require the scanning before neoadjuvant chemotherapy. Pooled sensitivities and specificities are listed in Table 2. Subgroup analysis was performed, by the time of scanning (during neoadjuvant chemotherapy and after neoadjuvant chemotherapy was completed).

Other reviews, including Li et al (2018), have also compared MRI with PET or PET/CT in evaluating response to neoadjuvant chemotherapy.[13,] Meta-analytic results are similar to previous studies and are presented in Table 2.

Table 2. Pooled Diagnostic Performance of FDG-PET and MRI in Detection of Residual Disease After Neoadjuvant Chemotherapy for Breast Cancer

Type of Imaging	No. of Studies (N)	Sensitivity (95% CI), %	Specificity (95% CI), %
Li et al (2018)[13,]			
MRI	13 (575)	88 (78 to 94)	69 (51 to 83)
FDG-PET or FDG-PET/CT	13 (618)	77 (58 to 90)	78 (63 to 88)
Xiao et al (2016)[10,]			
FDG-PET or FDG-PET/CT	26 (1752)	90 (88 to 90)	81 (78 to 84)
Liu et al (2016)[11,]			

Type of Imaging	No. of Studies (N)	Sensitivity (95% CI), %	Specificity (95% CI), %
MRI	6 (382)	65 (45 to 80)	88 (75 to 95)
FDG-PET or FDG-PET/CT	6 (382)	86 (76 to 93)	72 (49 to 87)
Sheikhbahaei et al (2016)[12,]			
All studies			
MRI	10 (492)	88 (76 to 95)	55 (41 to 68)
FDG-PET or FDG-PET/CT	10 (535)	71 (52 to 85)	77 (58 to 89)
FDG-PET/CT	7 (385)	82 (62 to 92)	79 (52 to 93)
FDG-PET	3 (150)	43 (26 to 63)	73 (44 to 91)
During neoadjuvant chemotherapy			
MRI	3 (256)	89 (66 to 97)	42 (20 to 68)
FDG-PET/CT	3 (256)	91 (86 to 95)	69 (25 to 93)
After neoadjuvant chemotherapy completion			
MRI	7 (236)	88 (71 to 96)	63 (51 to 74)
FDG-PET or FDG-PET/CT	7 (279)	57 (40 to 71)	80 (65 to 90)
FDG-PET/CT	4 (129)	71 (42 to 89)	88 (73 to 95)

CI: confidence interval; CT: computed tomography; FDG: fluorine 18 fluorodeoxyglucose; MRI: magnetic resonance imaging; PET: positron emission tomography.

Two 2012 meta-analyses pooled studies on the use of FDG-PET to predict pathologic response to neoadjuvant therapy before surgery for locally advanced breast cancer.[14,15,] Both reviews reported similar pooled point estimates for sensitivity and specificity. Both concluded that PET had reasonably high sensitivity and relatively low specificity. Neither described how PET should be used to influence patient management decisions and therefore whether health outcomes would be changed relative to decisions not based on PET results. Thus, it is unclear whether PET improves outcomes for predicting pathologic response to neoadjuvant therapy for locally advanced breast cancer.

Breast Cancer Estrogen Receptor Status

Several studies have investigated the use of FES-PET/CT to determine estrogen receptor (ER) status in individuals with recurrent or metastatic breast cancer.

Systematic Reviews

Kurland et al (2020) conducted a systematic review and primary meta-analysis on FES-PET of metastatic lesions including 113 nonbreast lesions from 4 studies.[16,] For the primary analysis of FES-PET/CT to detect ER-status from metastatic lesions, using immunohistochemistry (IHC) as the reference standard, found a sensitivity of 78% (95%CI, 65% to 88%) and specificity of 98%

(95% CI, 65% to 100%). The authors note limitations of this meta-analysis were that inclusion and exclusion criteria for patients and lesions were not clear in all studies and qualitative and quantitative thresholds for ^{18}F-FES positivity and ER status were not uniform across studies. The authors conclude that tissue sampling limitations, intrapatient heterogeneity, and temporal changes in molecular markers may make FES-PET a complement to existing assays.

Xu et al (2025) conducted a systematic review and meta-analysis of 21 studies evaluating the diagnostic and staging accuracy of FES-PET/CT.[17,] Ten studies evaluated the diagnostic capability of FES PET/CT compared to FDG PET and found FES-PET/CT to have a sensitivity of 0.75 (95% CI, 0.62 to 0.85) and a false-positive rate (PFR) of 0.27 (95% CI, 0.09 to 0.50). In terms of ER status detection, 8 studies found a pooled sensitivity of 0.86 (95% CI, 0.71 to 0.94) and the FPR was 0.45 (95% CI, 0.19 to 0.73). For predictive ability for endocrine therapy response, 12 studies found a pooled sensitivity of 0.79 (95% CI, 0.62 to 0.89) and an FPR of 0.58 (95% CI, 0.42 to 0.72).

Randomized Controlled Trials

Gennari et al (2024) conducted a pilot study of the use of FES-PET/CT in ER-positive/human epidermal growth factor receptor 2 (HER2)-negative metastatic breast cancer comparing first-line endocrine therapy (ET) versus chemotherapy (ChT) (N=147).[18,] 117 patients had FES-PET standardized uptake value (SUV) ≥2 and received ET, and 30 patients had SUV <2 and were randomized to ET (arm A) or ChT (arm B). These results demonstrated that FES-PET can be used to identify patients classified as endocrine resistant. Those with SUVmax <2 who received first-line chemotherapy had improved outcomes compared to first-line endocrine therapy. After median follow-up (62.4 months), 104 (73.2%) patients had disease progression and 53 (37.3%) died. Median progression free survival in patients with SUV <2 was 12.4 months (95% CI: 3.1 to 59.6) in patients randomized to arm A versus 23.0 months (95% CI: 3.1 to 59.6) in patients randomized to arm B. Median overall survival was 28.2 months (95% CI: 14.2 to not estimable) in arm A versus 52.8 months (95% CI: 16.2 to not estimabl) in arm B. The authors noted several limitations. 60-month OS rate was 41.6% (95% CI: 10.4% to 71.1%) in arm A, 42.0% (95% CI: 14.0% to 68.2%) in arm B, and 59.6% (95% CI: 48.6% to 69.0%) in patients with SUV ≥2. The study had slow and low accrual due to technical difficulties in activating an international, multicenter trial. Also, the percentage of patients with FES-PET SUV <2 was lower than expected according to available evidence at the time of study planning.

Nonrandomized Clinical Trials

Ulaner et al (2024) conducted a nonrandomized, single-center phase 2 trial on the use of FES-PET for initial staging and suspected recurrence in ER-positive breast cancer.[19,] Patients with ER-positive locally advanced breast cancer (cohort 1; n=62) or suspected recurrence (cohort 2; n=62) were enrolled. Patients underwent standard-of-care imaging (SOC) and FES-PET imaging. In cohort 1, of 14 true-positive findings, SOC detected 12 and FES-PET detected 11 (p>.99). In cohort 2, of 23 true-positive findings, SOC detected 16 and FES detected 18 (p=.77). These results showed no difference between SOC and FES-PET.

van Geel et al (2022) conducted a prospective study on the clinical validity of FES-PET/CT to assess ER status in newly diagnosed metastatic breast cancer (N=181).[20,] FES-PET/CT was compared to biopsy. The accuracy of FES-PET/CT to predict biopsied metastasis had a sensitivity of 95% (95% CI, 89% to 97%), a specificity of 80% (66% to 89%), a positive predictive value of 93% (95% CI, 87% to 96%), and a negative predictive value of 85% (95% CI, 72% to 92%).

These results demonstrated clinical validity of the use of FES-PET/CT to determine tumor ER status.

Chae et al (2019) conducted a prospective study on the diagnostic accuracy and safety of FES-PET/CT for the assessment of ER status in recurrent or metastatic lesions in patients with breast cancer (N=93).[21,] 47 (55%) were oestrogen receptor-positive and 38 (45%) were oestrogen receptor-negative. Positive status percent agreement between the FES-PET/CT results and estrogen receptor status by immunohistochemical assay was 76.6% (95% CI, 62.0% to 87.7%) and the negative status percent agreement was 100.0% (95% CI, 90.8% to 100.0%).

GUIDELINES

American College of Radiology

In 2019 , the ACR issued an Appropriateness Criteria for the initial workup and surveillance for local recurrence and distant metastases in asymptomatic women with stage I breast cancer.[22,] The ACR noted that FDG-PET/CT is usually not appropriate during initial workup or surveillance of these individuals to rule out metastases.

National Comprehensive Cancer Network

Current NCCN guidelines on breast cancer (v.4.2025) include a category 2B recommendation for FDG-PET/CT as an optional test in the workup of breast cancer.[23,] The use of FDG-PET/CT "may be helpful in situations where standard staging studies are equivocal or suspicious. FDG-PET/CT may also be helpful in identifying unsuspected regional nodal disease and/or distant metastases when used in addition to standard staging studies."

The NCCN states FES PET/CT may be considered for ER-positive disease and lobular histology. It does not state the clinical scenarios when FES-PET/CT should be used or which treatment decisions it may inform.

The NCCN recommends against routine use of FDG-PET/CT "in the staging of clinical stage I, II, or operable III (T3,N1) breast cancer due to its high false-negative rate for detection of lesions that are small (<1 cm) and/or low-grade disease, the high rate of false-positive scans in patients without locally advanced disease, the low sensitivity for detection of axillary nodal metastases, and the low probability of these patients having detectable metastatic disease."

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

Society of Nuclear Medicine and Molecular Imaging

In 2023, the Society of Nuclear Medicine and Molecular Imaging (SNMMI) issued Appropriate Use Criteria for ER-targeted PET imaging with FES.[24,] The working group determined FES-PET was appropriate in several clinical scenarios:

- "Assessing ER status in lesions that are difficult to biopsy or when biopsy is nondiagnostic;
- After progression of metastatic disease, for considering second line of endocrine therapy;
- At initial diagnosis of metastatic disease, for considering endocrine therapy;

- Detecting ER status when other imaging tests are equivocal or suggestive."

In 2025, the SNMMI published Appropriate Use Criteria for FDG-PET/CT for initial staging of malignant disease.[25,] The recommendations for breast cancer include:

- "...an appropriateness score of 8 (appropriate) in patients with stage IIB–IV NST [no special type] breast cancer and may replace systemic staging that uses conventional imaging modalities. This appropriateness applies regardless of receptor status and includes ER+, HER2+, and triple-negative tumors."
- "In patients with stage I–IIA, the appropriateness score was lowered to 3 (rarely appropriate)."

Section Summary: Breast Cancer

Evidence for the use of PET or PET/CT in individuals with breast cancer consists of TEC Assessments, systematic reviews, and meta-analyses. There is no evidence that PET is useful in diagnosing breast cancer. The false-negative rates of PET in individuals with breast cancer are estimated to be between 5.5% and 8.5%, which can be considered unacceptable, given that breast biopsy can provide more definitive results. Use of PET/CT might be useful in detecting metastases when results from other imaging techniques are inconclusive. The evidence supports the use of FDG-PET and FDG-PET/CT for staging and restaging only if standard staging methods are inconclusive.

The evidence does not support the use of FDG-PET and FDG-PET/CT for diagnosis, staging, and restaging when standard staging methods are conclusive.

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

The evidence does not support the use of FES-PET for individuals with breast cancer.

CERVICAL CANCER

Systematic Reviews

In a systematic review of 20 studies, Chu et al (2014) reported a pooled sensitivity and specificity for FDG-PET or FDG-PET/CT of 87% (95% CI, 80% to 92%) and 97% (95% CI, 96% to 98%), respectively, for distant metastasis in recurrent cervical cancer.[26,] For local-regional recurrence, pooled sensitivity and specificity were 82% (95% CI, 72% to 90%) and 98% (95% CI, 96% to 99%), respectively.

In a meta-analysis of 9 cervical cancer recurrence studies, Rong et al (2013) reported sensitivity and a specificity for PET/CT of 94.8% (95% CI, 91.2% to 96.9%) and 86.9% (95% CI, 82.2% to 90.5%), respectively.[8,] Reviewers found the quality of studies on recurrence was average with some limitations. For example, studies included mostly symptomatic women and did not differentiate between PET for diagnosis or surveillance.

An Agency for Healthcare Research and Quality (AHRQ) review (2008) identified several studies using FDG-PET or FDG-PET/CT to stage advanced cervical cancer and to detect and stage recurrent disease.[27,] The report concluded that most studies supported enhanced diagnostic accuracy, which would improve the selection of appropriate treatment for individuals. For

recurrent disease, PET identified additional sites of metastasis, which would alter treatment decisions in some cases. For example, in a study by Yen et al (2004) of 55 individuals whose recurrences were initially considered curable with radical surgical treatment, 27 instead underwent palliative therapy based on PET results.[28,] An NCCN report conducted by Podoloff et al (2009) also identified several studies supporting the use of PET for initial staging and identifying and staging recurrent disease.[29,]

Guidelines
Current NCCN guidelines on cervical cancer (v.4.2025) state that PET/CT may be considered under the following conditions:[30,]

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

Section Summary: Cervical Cancer
Evidence for the use of PET in individuals with cervical cancer consists of systematic reviews and meta-analyses. Pooled results have shown that PET can be used for staging or restaging and detecting recurrent disease. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of cervical cancer.

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

ENDOMETRIAL CANCER

Systematic Reviews
Bollineni et al (2016) published a systematic review and meta-analysis on the diagnostic value of FDG-PET for endometrial cancer.[31,] The literature search, conducted through August 2015, identified 21 studies for inclusion in the meta-analysis: 13 on detection of lymph node metastases (n=861) and 8 on detection of endometrial cancer recurrence (n=378). Pooled sensitivity and specificity for FDG-PET for detecting lymph node metastases were 72% (95% CI, 63% to 80%) and 94% (95% CI, 93% to 96%), respectively. Pooled sensitivity and specificity for FDG-PET for detecting endometrial cancer recurrence following primary surgical treatment were 95% (95% CI, 91% to 98%) and 91% (95% CI, 86% to 94%), respectively.

GUIDELINES

American College of Radiology
In 2020, the ACR issued Appropriateness Criteria for the pretreatment evaluation and follow-up of endometrial cancer.[32,] Skull base to mid-thigh PET/CT may be appropriate for pretreatment evaluation for lymph node and distant metastases, is usually appropriate for initial staging for high-grade tumors, and is usually appropriate for evaluation of clinically suspected recurrence of endometrial cancer.

National Comprehensive Cancer Network
Current NCCN guidelines on endometrial cancer (v.3.2025) state that PET/CT may be considered under the following conditions:[33,]

- Consider FDG-PET/CT if metastasis is suspected in select patients during initial workup for both nonfertility-sparing and fertility-sparing.
- PET/CT should cover neck, chest, abdomen, pelvis, and groin.
- Whole body FDG-PET/CT can be considered if suspected recurrence or metastasis.

Section Summary: Endometrial Cancer
The evidence includes a systematic review and meta-analysis. Pooled estimates from the meta-analysis showed high sensitivities and specificities for FDG-PET/CT in detecting lymph node metastases and endometrial cancer recurrence following treatment. The evidence supports the use of FDG-PET and PET/CT for the diagnosis, staging and restaging, or surveillance of endometrial cancer.

Ovarian Cancer
For primary evaluation (ie, suspected ovarian cancer), the ability to rule out malignancy with a high NPV would change management by avoiding unnecessary exploratory surgery. However, available studies have suggested that PET scanning has a poorer NPV than other options, including transvaginal ultrasound, Doppler studies, or MRI. Adding PET scan to ultrasound or MRI did not improve results.

PPV is of greatest importance in evaluating individuals with known ovarian cancer, either to detect disease recurrence or progression or to monitor response to treatment.

Systematic Reviews
A meta-analysis by Xu et al (2017) evaluated the diagnostic value of PET and PET/CT for recurrent or metastatic ovarian cancer.[34,] The literature search, conducted through August 2014, identified 64 studies for inclusion: 15 studies (n=657) using PET and 49 studies (n=3065) using PET/CT. The pooled sensitivity and specificity for PET were 89% (95% CI, 86% to 92%) and 90% (95% CI, 84% to 93%), respectively. The pooled sensitivity and specificity for PET/CT were 92% (95% CI, 90% to 93%) and 91% (95% CI, 89% to 93%), respectively. Subgroup analyses were conducted by study region (Asia, Europe, and America). For PET/CT, sensitivities in the Asia and Europe studies were significantly higher compared with the sensitivity in the America studies.

A meta-analysis by Limei et al (2013), included 28 studies (N=1651) published through December 2012; it evaluated the diagnostic value of PET/CT in suspected recurrent ovarian cancer.[35,] Using the Oxford Evidence rating system for quality, 7 studies were considered high quality and 21 were low-quality. Reviewers found PET/CT was useful for detecting ovarian cancer recurrence, with pooled sensitivity and specificity of 89% and 75% for the high-quality studies and 89% and 93% for the low-quality studies, respectively.

An AHRQ systematic review conducted by Matchar et al (2004) suggested that PET might have value for detecting recurrence when cancer antigen 125 is elevated and conventional imaging does not clearly show recurrence, this had not been demonstrated in an adequately powered prospective study.[36,] An AHRQ systematic review conducted by Ospina et al (2008) found that

evidence supported the use of PET/CT for detecting recurrent ovarian cancer.[27,] Evidence for initial diagnosis and staging of ovarian cancer was inconclusive.

A meta-analysis by Zou et al (2025) evaluated the diagnostic value of PET/CT for recurrent or metastatic ovarian cancer in postoperative patients with elevated serum CA125 levels.[37,] The literature search identified 13 studies (N=421) and found pooled sensitivity of 0.94 (95% CI, 0.91 to 0.97) and specificity of 0.83 (95% CI, 0.71 to 0.91). The pooled positive likelihood proportion was 4.59 (95% CI, 2.81 to 7.51), the pooled negative likelihood proportion was 0.09 (95% CI, 0.05 to 0.15), and the pooled diagnostic odds ratio was 64.22 (95% CI, 27.21 to 151.57).

A meta-analysis by Wang et al (2022) evaluated PET/CT in the recurrence of epithelial ovarian cancer. A total of 17 studies in 639 patients were evaluated.[38,] The sensitivity for the diagnosis of epithelial ovarian cancer recurrence was 0.88 (95% CI, 0.79 to 0.93) and the specificity was 0.89 (95% CI, 0.72 to 0.96).

GUIDELINES

American College of Radiology

In 2025 , the ACR published Appropriateness Criteria on staging and follow-up of ovarian cancer stating that PET/CT and MRI may be appropriate for pretreatment staging.[39,] FDG-PET/CT was reported as usually appropriate for posttreatment response evaluation while FDG-PET/MRI may be appropriate. These procedures may also be appropriate for posttreatment surveillance and FDG-PET/CT is usually appropriate for posttreatment evaluation.

National Comprehensive Cancer Network

Current NCCN guidelines for ovarian cancer (v.3.2025) indicate that PET/CT can be appropriate "for indeterminate lesions if results will alter management."[40,] Use of PET/CT may be considered for monitoring individuals with stage I through IV ovarian cancer receiving adjuvant chemotherapy or after initial treatment (eg, surgery followed by chemotherapy) if clinically indicated. PET/CT also can be considered if clinically indicated after complete remission, for follow-up and for monitoring for recurrence if cancer antigen 125 is rising or clinical relapse is suspected.

Section Summary: Ovarian Cancer

Evidence for PET and PET/CT for the initial diagnosis of ovarian cancer consists of an AHRQ systematic review (2008), which reported that the evidence is inconclusive. Evidence on the use of PET and PET/CT for the detection of ovarian cancer recurrence includes multiple meta-analyses and an AHRQ systematic review (2008). Pooled sensitivities and specificities support the use of PET and PET/CT for the detection of recurrent ovarian cancer. The evidence supports the use of FDG-PET and FDG-PET/CT for the diagnosis and staging and restaging of ovarian cancer.

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

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.

Table 3. National FDG PET Coverage for Oncologic Conditions

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

*Cervix: Nationally non-covered for the initial diagnosis of cervical cancer related to initial anti-tumor treatment strategy. All other indications for initial anti-tumor treatment strategy for cervical cancer are nationally covered.
*Breast: Nationally non-covered for initial diagnosis and/or staging of axillary lymph nodes. Nationally covered for initial staging of metastatic disease. All other indications for initial anti-tumor treatment strategy for breast cancer are

nationally covered.
*Melanoma: Nationally non-covered for initial staging of regional lymph nodes. All other indications for initial anti-tumor treatment strategy for melanoma are nationally covered.

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 (Table 4).

Table 4. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT06695039	A Phase 2, Open-label, Non-randomized, Single Center Study to Explore Diagnostic Performance of [18F]fluoroestradiol (FES) PET/CT for the Assessment of Axillary Lymph Node Metastasis in Estrogen-positive Breast Cancer	77	Dec 2026
NCT06877949	FDG-PET/CT Versus Conventional CT for Response Monitoring in Metastatic Breast Cancer: A Multicenter Randomized Clinical Trial (MONITOR-RCT)	420	Apr 2029
NCT06232122	Evaluation of 68Ga-FAPI-46 and 18F-FDG PET/CT Imaging for Detecting Recurrent Tumor Lesions in Patients of Ovarian Cancer With CA125 Elevation From Complete Response After Therapy	45	Jul 2028
NCT06072807	Brain [18F]-FES PET/CT in the Diagnosis, Treatment Planning and Response Assessment of Brain Metastases in Patients With Estrogen-Receptor Positive Breast Cancer	20	Dec 2026
NCT02285192	Positron Lymphography Via Intracervical 18F-FDG Injection for Pre-surgical Lymphatic Mapping in Stage IB1 Cervical Cancer and High-grade Endometrial Cancer	42	Nov 2025 (active, not recruiting)
NCT05824247	A Prospective Cohort Study of 68ga-FAPI-pet-ct Versus FDG-pet-ct for Ovarian Cancer	60	Jun 2025 (unknown status)
NCT05486182[a]	Impact of 18F-fluoroestradiol (FES) Positron Emission Tomography (PET) on the Therapeutic Treatment of Metastatic Breast Cancer Ipatients, Initially ER Positive and HER2 Negative, in Relapse After First-line Therapy Combining Hormone Therapy	153 (actual)	Jan 2026
NCT01737619	Prospective Evaluation of Lymph Node Metastasis At the Time of Surgical Staging for High Risk Endometrial Cancer	150	Dec 2025
NCT05088785	Dynamic and Test-retest Whole Body [18F]FES PET Imaging in Patients With Metastatic ER+ Breast Cancer	15	Apr 2025
NCT05613270	A Prospective Pilot Study to Explore Performance and Efficacy of 18F-FES PET/CT in ER-positive Breast Cancer Patients	50	Dec 2024

NCT No.	Trial Name	Planned Enrollment	Completion Date
NCT03442504	Evaluation Study of the Prediction of the Response to Second-line Hormone Therapy by 16α- [18F] Fluoro-17β-estradiol (FES) PET in Patients With Metastatic Breast Cancer	57 (actual)	Jun 2024 (active, not recruiting)
NCT05056259	Usefulness of 18F-FDG PET/CT in the Initial Staging and Surveillance of Endometrial Cancer Patients	42	Oct 2023 (unknown status)
Unpublished			
NCT01916122	Fluorestradiol (FES) PET/CT for Imaging Estrogen Receptor Status	54 (actual)	Apr 2024
Terminated			
NCT04727632	[18F]Fluoroestradiol-PET/CT Companion Imaging Study to the FORESEE: Functional Precision Oncology for Metastatic Breast Cancer Feasibility Trial	2 (actual)	Jul 2024 (terminated; it was not feasible to perform FES PET/CT)
NCT02149173	Serial [F-18] Fluoroestradiol (FES) PET Imaging to Evaluate Endocrine-Targeted Therapy	29 (actual)	Jan 2021 (terminated due to low accrual)
NCT02317302	FDG Tumor Heterogeneity During Chemoradiation as a Predictor of Response to Concurrent Radiation Therapy and Chemotherapy in Patients With Cervical Cancer	48 (actual)	Jun 2020 (terminated; insufficient funding)
NCT00816582	A Phase II Clinical Trial to Evaluate 18F-Fluoroestradiol Positron Emission Tomography / Computerized Tomography (PET/CT) Guided Fulvestrant Therapy for Patients With Recurrent or Metastatic Breast Cancer	17 (actual)	Jul 2018 (terminated; slow accrual)

NCT: national clinical trial.
[a] Denotes industry-sponsored or cosponsored trial.

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	
78608	Brain imaging, positron emission tomography (PET); metabolic evaluation
78609	Brain imaging, positron emission tomography (PET); perfusion evaluation
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
A9591	Fluoroestradiol F-18, diagnostic, 1 mCi
A9552	Fluorodeoxyglucose F-18 FDG, diagnostic, per study dose, up to 45 millicuries
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
G0235	PET imaging, any site not otherwise specified
G0252	PET imaging, full and partial-ring PET scanners only, for initial diagnosis of breast cancer and/or surgical planning for breast cancer (eg, initial staging of axillary lymph nodes).

REVISIONS	
Posted 01-28-2025 Effective 02-27-2025	Oncologic Applications Breast and Gynecologic was originally part of the Positron Emission Tomography (PET) Scanning: Oncologic Applications medical policy. Oncologic Applications for Breast and Gynecologic has been pulled out and placed into a separate medical policy, Positron Emission Tomography (PET) Scanning: Oncologic Applications (Breast and Gynecologic). The medical policy language was updated with the changes noted below.
	Updated Description section.

REVISIONS	
	Updated Policy Section ▪ Section A Breast Cancer Added: "using ^{18}F-FDG isotope" to section A1 and A2 ▪ Added Section A3: "PET scanning using fluoroestradiol F18 (FES) is considered experimental / investigational in individuals with breast cancer (see Policy Guidelines for exceptions)" ▪ Section B Cervical Cancer Added: "using ^{18}F-FDG isotope" to section B1 and B2 ▪ Section C Endometrial Cancer Added: "using ^{18}F-FDG isotope" to section C1 ▪ Section D Ovarian Cancer Added: "using ^{18}F-FDG isotope" to section D1 and D2
	Updated Policy Guidelines ▪ Added Policy Guideline D: "Use of fluoroestradiol F18 (FES)-PET may be considered in individuals with recurrent or metastatic breast cancer in certain clinical scenarios, such as when a biopsy is inconclusive. Current NCCN guidelines on breast cancer (v.5.2024) state that FES-PET may be considered for estrogen receptor-positive disease."
	Updated Rationale section.
	Updated Coding section. ▪ Added A9591
	Updated Reference section.
01-13-2026	Updated Description Section
	Updated Policy Section ▪ Removed: All policy statements apply to both positron emission tomography (PET) scans and PET plus computed tomography (CT) scans (ie, 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.
	Updated Policy Guidelines Section ▪ Removed: Patient Selection: As with any imaging technique, the medical necessity of positron emission tomography (PET) scanning depends in part on what imaging techniques are used before or after the PET scanning. Due to its expense, PET scanning is typically considered after other techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), or ultrasonography, provide inconclusive or discordant results. 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, including situations when an individual has a contraindication to intravenous contrast agents, making initial CT scans unattainable. Selection criteria for PET scanning may also be complex. 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.

REVISIONS	
	Use of fluoroestradiol F18 (FES)-PET may be considered in individuals with recurrent or metastatic breast cancer in certain clinical scenarios, such as when a biopsy is inconclusive. Current NCCN guidelines on breast cancer (v.5.2024) state that FES-PET may be considered for estrogen receptor-positive disease. ▪ Added: 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.
	Updated Rationale Section
	Updated Reference Section

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