BlueCross BlueShield Federal Employee Program.

FEP Medical Policy Manual

FEP 6.01.66 Oncologic Applications of Positron Emission Tomography Scanning (Thyroid, Neuroendocrine, Head and Neck)

Annual Effective Policy Date: October 1, 2024

Original Policy Date: September 2024

Related Policies:

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
6.01.60 - Therapeutic Radiopharmaceuticals for Neuroendocrine Tumors
6.01.62 - Oncologic Applications of Positron Emission Tomography Scanning (Breast and Gynecologic)
6.01.63 - Oncologic Applications of Positron Emission Tomography Scanning (Bone and Sarcoma)
6.01.64 - Oncologic Applications of Positron Emission Tomography Scanning (Hematologic)
6.01.65 - Oncologic Applications of Positron Emission Tomography Scanning (Lung)
6.01.67 - Oncologic Applications of Positron Emission Tomography Scanning (Brain, Melanoma, Unknown Primary)

Oncologic Applications of Positron Emission Tomography Scanning (Thyroid, Neuroendocrine, Head and Neck)

Description

Description

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

OBJECTIVE

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

POLICY STATEMENT

Head and Neck Cancer

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

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

Neuroendocrine Tumors

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

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

Thyroid Cancer

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

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

Cancer 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

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.

Patient selection criteria for PET scanning may also be complex. Due to the complicated hierarchy of imaging options in individuals with malignancy and complex patient selection criteria, a possible implementation strategy for this policy is its use for retrospective review, possibly focusing on cases with multiple imaging tests, including PET scans.

Use of PET scanning for surveillance as described in the policy statement and policy rationale refers to the use of PET to detect disease in asymptomatic 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.

Coding

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

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

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

PI - Positron emission tomography (PET) or PET/computed tomography (CT) to inform the initial treatment strategy of tumors that are biopsy proven or strongly suspected of being cancerous based on other diagnostic testing, 1 per cancer diagnosis.

PS - Positron emission tomography (PET) or PET/computed tomography (CT) to inform the subsequent treatment strategy of cancerous tumors when the beneficiary's treating physician determines that the PET study is needed to inform subsequent anti-tumor strategy.

BENEFIT APPLICATION

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

FDA REGULATORY STATUS

As of October 2023, the following radiopharmaceuticals have been granted approval by the FDA, to be used with PET for head and neck, neuroendocrine, or thyroid cancer-related indications (see Table 1).[1,]

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

Radiopharmaceutical	Manufacturer	Name	Carcinoma-Related Indication With PET
Copper-64 dotatate	Curium	Detectnet™	Localization of somatostatin receptor-positive NETs in adult individuals
Fluorine-18 fluorodeoxyglucose (FDG)	Various		Suspected or existing diagnosis of cancer, all types
Gallium-68 dotatoc	UIHC - P E T Imaging Center		Localization of somatostatin receptor-positive NETs in adult and pediatric individuals
Gallium-68 dotatate	Advanced Accelerator Applications	NETSPOT™	Localization of somatostatin receptor-positive NETs in adult and pediatric individuals

NET: neuroendocrine tumors.

RATIONALE

Summary of Evidence

Head and Neck Cancer

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

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

Neuroendocrine Tumors

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

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

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

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

Thyroid Cancer

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

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

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, effective for claims with dates of service on and after June 11, 2013, is summarized in Table 2.[29,]

Table 2. 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.

REFERENCES

1. Riberich R. FDA-Approved PET Radiopharmaceuticals. http://www.radiopharmaceuticals.info/pet-radiopharmaceuticals.html. Accessed November 1, 2023.
2. Chen WS, Li JJ, Hong L, et al. Comparison of MRI, CT and 18F-FDG PET/CT in the diagnosis of local and metastatic of nasopharyngeal carcinomas: an updated meta analysis of clinical studies. Am J Transl Res. 2016; 8(11): 4532-4547. PMID 27904660
3. Wei J, Pei S, Zhu X. Comparison of 18F-FDG PET/CT, MRI and SPECT in the diagnosis of local residual/recurrent nasopharyngeal carcinoma: A meta-analysis. Oral Oncol. Jan 2016; 52: 11-7. PMID 26547126
4. Cheung PK, Chin RY, Eslick GD. Detecting Residual/Recurrent Head Neck Squamous Cell Carcinomas Using PET or PET/CT: Systematic Review and Meta-analysis. Otolaryngol Head Neck Surg. Mar 2016; 154(3): 421-32. PMID 26715675
5. Sheikhbahaei S, Taghipour M, Ahmad R, et al. Diagnostic Accuracy of Follow-Up FDG PET or PET/CT in Patients With Head and Neck Cancer After Definitive Treatment: A Systematic Review and Meta-Analysis. AJR Am J Roentgenol. Sep 2015; 205(3): 629-39. PMID 26295652
6. Sheikhbahaei S, Ahn SJ, Moriarty E, et al. Intratherapy or Posttherapy FDG PET or FDG PET/CT for Patients With Head and Neck Cancer: A Systematic Review and Meta-analysis of Prognostic Studies. AJR Am J Roentgenol. Nov 2015; 205(5): 1102-13. PMID 26496559
7. Rohde M, Dyrvig AK, Johansen J, et al. 18F-fluoro-deoxy-glucose-positron emission tomography/computed tomography in diagnosis of head and neck squamous cell carcinoma: a systematic review and meta-analysis. Eur J Cancer. Sep 2014; 50(13): 2271-9. PMID 25011659
8. Yi X, Fan M, Liu Y, et al. 18 FDG PET and PET-CT for the detection of bone metastases in patients with head and neck cancer. A meta-analysis. J Med Imaging Radiat Oncol. Dec 2013; 57(6): 674-9. PMID 24283555
9. Gao S, Li S, Yang X, et al. 18FDG PET-CT for distant metastases in patients with recurrent head and neck cancer after definitive treatment. A meta-analysis. Oral Oncol. Mar 2014; 50(3): 163-7. PMID 24368204
10. Helsen N, Van den Wyngaert T, Carp L, et al. FDG-PET/CT for treatment response assessment in head and neck squamous cell carcinoma: a systematic review and meta-analysis of diagnostic performance. Eur J Nucl Med Mol Imaging. Jun 2018; 45(6): 1063-1071. PMID 29478080
11. Li Q, Zhang J, Cheng W, et al. Prognostic value of maximum standard uptake value, metabolic tumor volume, and total lesion glycolysis of positron emission tomography/computed tomography in patients with nasopharyngeal carcinoma: A systematic review and meta-analysis. Medicine (Baltimore). Sep 2017; 96(37): e8084. PMID 28906411
12. Lin J, Xie G, Liao G, et al. Prognostic value of 18F-FDG-PET/CT in patients with nasopharyngeal carcinoma: a systematic review and meta-analysis. Oncotarget. May 16 2017; 8(20): 33884-33896. PMID 27980228
13. Blue Cross Blue Shield Association Technology Evaluation Center (TEC). FDG Positron Emission Tomography in Head and Neck Cancer. Technol Eval Cent Assess. 2000;15(4).
14. Zhu Y, McLaren O, Hardman J, et al. Systematic review and meta-analysis of the diagnostic effectiveness of positron emission tomography-computed tomography versus magnetic resonance imaging in the post-treatment surveillance of head and neck squamous cell carcinoma. J Laryngol Otol. Jan 2023; 137(1): 22-30. PMID 35086577
15. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Head and Neck Cancers. Version 1.2024. https://www.nccn.org/professionals/physician_gls/pdf/head-and-neck.pdf. Accessed October 30, 2023.
16. Barrio M, Czernin J, Fanti S, et al. The Impact of Somatostatin Receptor-Directed PET/CT on the Management of Patients with Neuroendocrine Tumor: A Systematic Review and Meta-Analysis. J Nucl Med. May 2017; 58(5): 756-761. PMID 28082438
17. Deppen SA, Blume J, Bobbey AJ, et al. 68Ga-DOTATATE Compared with 111In-DTPA-Octreotide and Conventional Imaging for Pulmonary and Gastroenteropancreatic Neuroendocrine Tumors: A Systematic Review and Meta-Analysis. J Nucl Med. Jun 2016; 57(6): 872-8. PMID 26769864
18. Treglia G, Castaldi P, Rindi G, et al. Diagnostic performance of Gallium-68 somatostatin receptor PET and PET/CT in patients with thoracic and gastroenteropancreatic neuroendocrine tumours: a meta-analysis. Endocrine. Aug 2012; 42(1): 80-7. PMID 22350660
19. Treglia G, Cocciolillo F, de Waure C, et al. Diagnostic performance of 18F-dihydroxyphenylalanine positron emission tomography in patients with paraganglioma: a meta-analysis. Eur J Nucl Med Mol Imaging. Jul 2012; 39(7): 1144-53. PMID 22358431

20. Delpassand ES, Ranganathan D, Wagh N, et al. 64 Cu-DOTATATE PET/CT for Imaging Patients with Known or Suspected Somatostatin Receptor-Positive Neuroendocrine Tumors: Results of the First U.S. Prospective, Reader-Masked Clinical Trial. J Nucl Med. Jun 2020; 61(6): 890-896. PMID 31924723
21. Johnbeck CB, Knigge U, Loft A, et al. Head-to-Head Comparison of 64 Cu-DOTATATE and 68 Ga-DOTATOC PET/CT: A Prospective Study of 59 Patients with Neuroendocrine Tumors. J Nucl Med. Mar 2017; 58(3): 451-457. PMID 27660147
22. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Neuroendocrine and Adrenal Tumors. Version 1.2023. https://www.nccn.org/professionals/physician_gls/pdf/neuroendocrine.pdf. Accessed October 31, 2023.
23. Schtz F, Lautenschlger C, Lorenz K, et al. Positron Emission Tomography (PET) and PET/CT in Thyroid Cancer: A Systematic Review and Meta-Analysis. Eur Thyroid J. Jan 2018; 7(1): 13-20. PMID 29594049
24. Haslerud T, Brauckhoff K, Reister L, et al. F18-FDG-PET for recurrent differentiated thyroid cancer: a systematic meta-analysis. Acta Radiol. Oct 2016; 57(10): 1193-200. PMID 26163534
25. Podoloff DA, Ball DW, Ben-Josef E, et al. NCCN task force: clinical utility of PET in a variety of tumor types. J Natl Compr Canc Netw. Jun 2009; 7 Suppl 2: S1-26. PMID 19555588
26. Pace L, Klain M, Salvatore B, et al. Prognostic role of 18F-FDG PET/CT in the postoperative evaluation of differentiated thyroid cancer patients. Clin Nucl Med. Feb 2015; 40(2): 111-5. PMID 25546215
27. Cheng X, Bao L, Xu Z, et al. ⁸F-FDG-PET and ⁸F-FDG-PET/CT in the detection of recurrent or metastatic medullary thyroid carcinoma: a systematic review and meta-analysis. J Med Imaging Radiat Oncol. Apr 2012; 56(2): 136-42. PMID 22498184
28. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Thyroid Carcinoma. Version 4.2023. https://www.nccn.org/professionals/physician_gls/pdf/thyroid.pdf. Accessed November 1, 2023.
29. Centers for Medicare & Medicaid Services (CMS). 2013. Pub 100-03 National Coverage Determination (NCD) for Positron Emission TOMOGRAPHY (FDG) for Oncologic Conditions (220.6.17); https://tinyurl.com/7hc7hvpr. Accessed November 1, 2023.

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

Date	Action	Description
September 2024	New policy- Add to Radiology/Interventional Radiology section	Policy created by separating out head and neck, neuroendocrine, and thyroid indications from policy 6.01.26. Policy revised with literature review through October 13, 2023. No references added. Policy statements unchanged.