Positron Emission Tomography (PET) Scan

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INSTRUCTIONS:

“Medical Policy assists in administering UCare benefits when making coverage determinations for members under our health benefit plans. When deciding coverage, all reviewers must first identify enrollee eligibility, federal and state legislation or regulatory guidance regarding benefit mandates, and the member specific Evidence of Coverage (EOC) document must be referenced prior to using the medical policies. In the event of a conflict, the enrollee’s specific benefit document and federal and state legislation and regulatory guidance supersede this Medical Policy. In the absence of benefit mandates or regulatory guidance that govern the service, procedure or treatment, or when the member’s EOC document is silent or not specific, medical policies help to clarify which healthcare services may or may not be covered. This Medical Policy is provided for informational purposes and does not constitute medical advice. In addition to medical policies, UCare also uses tools developed by third parties, such as the InterQual Guidelines®, to assist us in administering health benefits. The InterQual Guidelines are intended to be used in connection with the independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice. Other Policies and Coverage Determination Guidelines may also apply. UCare reserves the right, in its sole discretion, to modify its Policies and Guidelines as necessary and to provide benefits otherwise excluded by medical policies when necessitated by operational considerations.”
POLICY DESCRIPTION:

This policy describes the use of positron emission tomography (PET), a three-dimensional nuclear imaging technique that measures the level of physiologic and biochemical activity or other organic function in an organ or tissue by reflecting the distribution of a radiotracer that has been administered to the patient. PET has been proposed as a method for diagnosing and predicting disease occurrence, staging a disease, and monitoring and predicting response to treatments.

COVERAGE RATIONALE / CLINICAL CONSIDERATIONS:

Positron emission tomography (PET) is considered **PROVEN and MEDICALLY NECESSARY** for diagnosis, staging, restaging, treatment and monitoring of the following types of **cancer**:

- Colorectal,
- Esophagus,
- Head and neck (not thyroid or CNS),
- Lymphoma,
- Non-small cell lung,
- Ovary,
- Brain,
- Cervix,
- Small cell lung,
- Soft tissue sarcoma,
- Pancreas,
- Testes,
- Thyroid,
- Breast (male and female),
- Melanoma,
- Myeloma,
- All solid tumors with the exceptions of
  - Prostate,
  - Kidney,
  - Bladder,
  - Basal and squamous cell skin cancers.

Positron emission tomography (PET) is considered **EXPERIMENTAL and INVESTIGATIONAL** for any use in:

- Prostate,
- Kidney,
- Bladder,
- Basal and squamous cell skin cancers.

Positron emission tomography (PET) is considered **PROVEN and MEDICALLY NECESSARY** for assessing:

- Myocardial viability in patients with **coronary artery disease (CAD)**,
- **Left ventricular dysfunction (LVD)** in patients who are being considered for revascularization.
Positron emission tomography (PET) is considered PROVEN and MEDICALLY NECESSARY for diagnosing and/or determining the severity of CAD in symptomatic patients with suspected or known CAD and any of the following conditions:

- Single photon emission computed tomography (SPECT) is unavailable or inconclusive,
- Body habitus or other conditions which can lead to an indeterminate SPECT, e.g., obesity, large breasts, left mastectomy, breast implant, chest wall deformity, left pleural or pericardial effusion, circulatory problems in inferior-septal areas of the heart or other technical difficulty, such as an extensive prior myocardial infarction,
- Conditions for which angiography may be technically challenging, e.g., low to intermediate probability of CAD, borderline stenosis,
- Conditions associated with high risk for morbidity, e.g., allergy to contrast medium, poor arterial access or renal dysfunction.

Positron emission tomography (PET) is considered PROVEN and MEDICALLY NECESSARY for localizing seizure focus in patients meeting the following criteria:

- Medically refractory epilepsy,
- Results using conventional techniques for localizing seizure focus have been negative, nondiagnostic or discordant.

Positron emission tomography (PET) is considered PROVEN and MEDICALLY NECESSARY for assessing treatment effects in patients with epilepsy.

Positron emission tomography (PET) with amyloid imaging is considered PROVEN and MEDICALLY NECESSARY for the use of diagnosis and treatment assessment of Alzheimer’s disease (AD) in patients with cognitive and behavioral symptoms who meet ALL of the following criteria:

- Member is less than 65 years of age,
- Symptoms have been present for at least 12 months,
- Symptoms interfere with the ability to function at work or at usual activities,
- Symptoms represent a decline from previous level of functioning,
- Symptoms are not explained by delirium, psychiatric, cerebrovascular, or other neurologic disorder,
- Symptoms involve at least TWO of the following domains:
  - Impaired learning and the ability to acquire and remember new information,
  - Impaired reasoning, judgment, and performance of complex tasks,
  - Impaired visuospatial abilities,
  - Impaired language function,
  - Change in personality, behavior or comportment.

Positron emission tomography (PET) with amyloid imaging is considered EXPERIMENTAL and INVESTIGATIONAL for the diagnosis and treatment assessment of Alzheimer’s disease (AD) in the following circumstances:

- Patients who are asymptomatic
• Patients older than 65 who meet core clinical criteria* for probable AD,
• To determine severity of dementia,
• To evaluate the significance of a positive family history of dementia or the presence of apolipoprotein E,
• Patients with a cognitive complaint that is unconfirmed on clinical examination,
• To evaluate asymptomatic patients with suspected or confirmed personal or family history of pertinent autosomal mutation status,
• Nonmedical evaluation, such as legal situations, insurance coverage, employment screening or competence determinations.

Positron emission tomography (PET) is considered EXPERIMENTAL and INVESTIGATIONAL for the assessment of patients with autism spectrum disorders (ASDs) due to insufficient evidence published in peer-reviewed medical literature.

**Clinical Considerations:**

Typically, PET using radiotracer $^{18}$F-FDG is undertaken only if blood glucose is $\leq 150$ milligrams per deciliter (mg/dL), since higher blood glucose levels may interfere with $^{18}$F-FDG uptake in tissue.

* Core clinical criteria for probable AD (McKhann et al., 2011):
  • Symptoms interfere with the ability to function at work or at usual activities,
  • Symptoms represent a decline from previous level of functioning,
  • Symptoms are not explained by delirium, psychiatric, cerebrovascular, or other neurologic disorder,
  • Symptoms involve at least TWO of the following domains:
    • Impaired learning and the ability to acquire and remember new information,
    • Impaired reasoning, judgment, and performance of complex tasks,
    • Impaired visuospatial abilities,
    • Impaired language function,
    • Change in personality, behavior or comportment.

**BACKGROUND:**

Positron emission tomography (PET) is a 3-dimensional imaging technique that evaluates the level of physiological and biochemical activity within tissue cells by measuring the distribution of an injected or inhaled radiotracer. Due to differences in metabolic rates, the concentration of radiotracers within cancerous cells differs from the concentration in the surrounding normal tissue cells. PET has been proposed as an imaging tool for detection or confirmation of a variety of tumor types. Its value for oncology purposes is primarily based on its ability to image metabolic activity and the fact that the rate of some metabolic processes is increased in malignant tissue, compared with that in normal tissue.

The ability of PET to image metabolic activity makes it a valuable tool in oncology due to the increased rate
of some metabolic processes in malignant tissue as compared with that in normal tissue. Compared with normal tissue, malignant tissue is characterized by an increase in the regulatory enzymes of glycolysis, particularly hexokinase, and in the rate of glucose metabolism and transport.

For cardiac applications, PET has been used primarily in patients with known or suspected coronary artery disease (CAD). For diagnosing and evaluating CAD, cardiac catheterization with coronary angiography and ventriculography is the gold standard. This invasive procedure usually is preceded by noninvasive tests, each of which can detect at least one characteristic of CAD, such as ischemia, stenosis, reduced myocardial blood flow (MBF), or left ventricular dysfunction (LVD). PET measurement of myocardial blood flow, metabolism, or neuronal function has been used for assessing the effects of treatment for heart disease.

For neurological applications, PET, particularly with fluorine-18-labeled fluorodeoxyglucose (FDG or \(^{18}\text{F-FDG}\)) as a radiotracer, is a valuable technique for evaluating the cerebral metabolic rate in a variety of neurologic disorders and for differentiating between a variety of degenerative movement disorders and dementias. Since abnormalities in cerebral blood flow (CBF) frequently parallel metabolic abnormalities, CBF studies with PET may provide adequate data for the differential diagnosis of dementias.

Probable Alzheimer’s disease (AD) is diagnosed by findings of a comprehensive clinical evaluation; a definitive diagnosis of AD can only be obtained by autopsy (Kepe et al., 2006; Small et al., 2006). The clinical diagnosis of AD is especially difficult because of the heterogeneous nature of AD and because AD can manifest similarly or coexist with other forms of dementia, such as vascular dementia (VaD), dementia with Lewy bodies (DLB), Lewy body variant of AD (LBVAD), frontotemporal dementia (FTD)/frontotemporal lobar degeneration (FTLD and mild cognitive impairment (MCI). Several newly developed radiolabeled compounds targeting β-amyloid plaques, one of the major pathologic biomarkers of AD, have recently become available for clinical use and is being studied as a means of acquiring information to aid in the diagnosis and management of AD.

Because autism and other autistic spectrum disorders (ASD)s are associated with neurological dysfunction, PET has been investigated for assessment of brain function.

**REGULATORY STATUS:**

1. **U.S. FOOD AND DRUG ADMINISTRATION (FDA):**

   The FDA has cleared several stand-alone positron emission tomography (PET) systems as substantially equivalent to legally marketed predicate devices through its Center for Devices and Radiological Health (CDRH) 510(k) clearance process (search KPS in the Product Code field: click here). Some examples of the systems that have received FDA clearance during the last 10 years include, but are not limited to, the following:

   - PEM 2400 PET (PEM Technologies); K032063; issued August 18, 2003.
   - C-PET Plus (Philips Medical Systems Inc.); K042839; issued October 29, 2004.
   - PEMFlex Solo II High Resolution PET (Naviscan Inc.); K090553; issued March 31, 2009.
   - Attrius Truesight PET (Neusoft Positron Medical Systems Co. Ltd.); K090178; issued April 24, 2009.
   - ECAT II Positron Tomograph (currently manufactured by Siemens Healthcare; previously manufactured by Life Sciences).
• ECAT 953b Tomography (currently manufactured by Siemens Healthcare; previously manufactured by CTI PET Systems).
• ECAT Exact HR+ 962 camera (currently manufactured by Siemens Healthcare; previously manufactured by CTI PET Systems Inc.); K962797; approved October 15, 1996 CDRH, 1996.

Regulation of PET centers and PET radiopharmaceutical production has been the focus of considerable and ongoing controversy. According to the PET Drug Products – Current Good Manufacturing Practice (CGMP) document, variations in manufacturing practices can significantly affect safety and efficacy. The short half-life of most PET compounds limits the duration of their efficacy, which in turn limits the distance between the production location and the location where the drug can be used. The document also contains recommendations for staffing, quality assurance, facility design, equipment, production and process controls, laboratory controls, isotope, stability testing, acceptance criteria for the finished product, labeling and packaging, distribution, and recordkeeping. The FDA announced that as of December 12, 2011, commercial producers of PET drugs, including fluorine-18-labeled 2-deoxy-2-fluoro-D-glucose (\(^{18}\text{F-FDG}\)), are expected to submit New Drug Applications (NDAs) or Abbreviated New Drug Applications (ANDAs) for marketing approval. On February 2012, the FDA issued 2 draft guidance documents intended to help producers of PET drugs meet the requirements for the FDA drug approval process. The first draft guidance summarizes the Investigational New Drug (IND) process for unapproved PET drugs, makes recommendations on how to submit an IND, provides advice on investigational PET drug access options, and describes the process for requesting permission to charge for an investigational PET drug. The second draft guidance provides questions and answers that address nearly all aspects of the drug regulatory process, including application submission, review, compliance with CGMPs, inspections, registration and listing, and user fees. A list of other relevant CGMP documents is also available:

• PET Drug Products – Current Good Manufacturing Practice (CGMP) (PDF – 399KB) issued on December 9, 2009.
• Positron Emission Tomography (PET): Questions and Answers about CGMP Regulations for PET Drugs issued on December 9, 2009.
• Federal Register Notice: Final Rule – CGMP for PET Drugs issued on December 10, 2009.
• Positron Emission Tomography (PET): Additional Questions and Answers Based on December 9, 2009 Stakeholder Call issued on April 8, 2010.
• Small Entity Compliance Guide: PET Drugs – Current Good Manufacturing Practice (CGMP) (PDF – 228KB) issued in August 2011.

Radiopharmaceuticals used in PET imaging require FDA approval. Examples that have been found safe and effective by FDA standards include:

• \(^{13}\text{N-ammonia}\) for assessing myocardial perfusion under rest or pharmacological stress conditions in patients with suspected or existing coronary artery disease.
• \(^{18}\text{F-FDG}\) in combination with myocardial perfusion imaging for identifying myocardial hibernation in patients with coronary artery disease and left ventricular dysfunction.
• \(^{18}\text{F-FDG}\) for evaluating malignancy in patients with known or suspected abnormalities found with other imaging techniques or patients with an existing diagnosis of cancer.
• \(^{18}\text{F-FDG}\) for diagnosing seizure disorders.
2. CENTERS FOR MEDICARE AND MEDICAID SERVICES (CMS):

CMS continues to believe that the evidence is adequate to determine that the results of FDG PET imaging are useful in determining the appropriate initial anti-tumor treatment strategy for beneficiaries with suspected cancer and improve health outcomes and thus are reasonable and necessary under §1862(a)(1)(A) of the Social Security Act (the Act).

Therefore, CMS continues to nationally cover one FDG PET study for beneficiaries who have cancers that are biopsy proven or strongly suspected based on other diagnostic testing when the beneficiary’s treating physician determines that the FDG PET study is needed to determine the location and/or extent of the tumor for the following therapeutic purposes related to the initial anti-tumor treatment strategy:

- To determine whether or not the beneficiary is an appropriate candidate for an invasive diagnostic or therapeutic procedure; or
- To determine the optimal anatomic location for an invasive procedure; or
- To determine the anatomic extent of tumor when the recommended anti-tumor treatment reasonably depends on the extent of the tumor.

**Initial Anti-Tumor Treatment Strategy Nationally Covered Indications**

- CMS continues to nationally cover FDG PET imaging for the initial anti-tumor treatment strategy for male and female breast cancer only when used in staging distant metastasis.
- CMS continues to nationally cover FDG PET to determine initial anti-tumor treatment strategy for melanoma other than for the evaluation of regional lymph nodes.
- CMS continues to nationally cover FDG PET imaging for the detection of pre-treatment metastasis (i.e., staging) in newly diagnosed cervical cancers following conventional imaging.

**Initial Anti-Tumor Treatment Strategy Nationally Non-Covered Indications**

- CMS continues to nationally non-cover initial anti-tumor treatment strategy in Medicare beneficiaries who have adenocarcinoma of the prostate.
- CMS continues to nationally non-cover FDG PET imaging for diagnosis of breast cancer and initial staging of axillary nodes.
- CMS continues to nationally non-cover FDG PET imaging for initial anti-tumor treatment strategy for the evaluation of regional lymph nodes in melanoma.
- CMS continues to nationally non-cover FDG PET imaging for the diagnosis of cervical cancer related to initial anti-tumor treatment strategy.

**Subsequent Anti-Tumor Treatment Strategy Nationally Covered Indications**

Three FDG PET scans are nationally covered when used to guide subsequent management of anti-tumor treatment strategy after completion of initial anti-cancer therapy. Coverage of more than three FDG PET scans to guide subsequent management of anti-tumor treatment strategy after completion of initial anti-cancer therapy shall be determined by the local Medicare Administrative Contractors. Effective for claims with dates of service on and after June 11, 2013, the chart below summarizes national FDG PET coverage for oncologic conditions:
<table>
<thead>
<tr>
<th>FDG PET for Cancers</th>
<th>Initial Treatment Strategy (formerly “diagnosis” &amp; “staging”)</th>
<th>Subsequent Treatment Strategy (formerly “restaging” &amp; “monitoring response to treatment”)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colorectal</td>
<td>Cover</td>
<td>Cover</td>
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<tr>
<td>Esophagus</td>
<td>Cover</td>
<td>Cover</td>
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<tr>
<td>Head and Neck (not thyroid, CNS)</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Non-small cell lung</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Ovary</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Brain</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Cervix</td>
<td>Cover with exceptions *</td>
<td>Cover</td>
</tr>
<tr>
<td>Small cell lung</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Soft tissue sarcoma</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Testes</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Prostate</td>
<td>Non-cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Thyroid</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Breast (male and female)</td>
<td>Cover with exceptions *</td>
<td>Cover</td>
</tr>
<tr>
<td>Melanoma</td>
<td>Cover with exceptions *</td>
<td>Cover</td>
</tr>
<tr>
<td>All other solid tumors</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>Myeloma</td>
<td>Cover</td>
<td>Cover</td>
</tr>
<tr>
<td>All other cancers not listed</td>
<td>Cover</td>
<td>Cover</td>
</tr>
</tbody>
</table>

*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.

Medicare/Medicaid coverage is approved for $^{18}$F-FDG PET for localizing seizure focus in the presurgical
evaluation of refractory seizures when an FDA-approved full-ring or partial-ring PET scanner is used.

Centers for Medicare & Medicaid Services (CMS): Currently, Medicare coverage is approved for rubidium-82 (82Rb) PET at rest or with pharmacological stress for myocardial perfusion studies in patients with known or suspected CAD, when it is performed either in place of SPECT or when SPECT is inconclusive, defined as equivocal, technically uninterpretable, or discordant with other data. Imaging with a gamma camera system, however, is not covered. Medicare coverage also is approved for 18F-FDG PET for assessing myocardial viability prior to revascularization, either as the primary or initial diagnostic study or after inconclusive SPECT but only when undertaken with an FDA-approved full-ring or partial-ring PET scanner. Additionally, CMS recently announced its intent to begin approving coverage for 13NH3 PET alone or with stress for myocardial perfusion studies when performed in place of SPECT or after inconclusive SPECT. Implementation of coverage for 13NH3 PET will begin when the new policy is published in the Coverage Issues Manual, which also will provide any restrictions to coverage (CMS, 2003b).

Section 220.6 of the National Coverage Determination Manual identified five tracers as the only nationally covered radioisotopes for certain defined uses of PET. Certain uses of PET with these radioisotopes are covered only when performed under Coverage with Evidence Development (CED) in clinical studies. All remaining uses of PET are nationally noncovered, including tracers that allow for imaging of beta amyloid plaques in the brain of patients with cognitive impairment who are being evaluated for possible Alzheimer's disease or other causes of cognitive decline. In 2012, the Food and Drug Administration (FDA) approved a new tracer—florbetapir F18 injection (Amyvid®; Eli Lilly and Co.)—for the estimation of beta amyloid plaque density in patients with cognitive impairment being evaluated for Alzheimer’s disease and other causes of cognitive decline.

The Centers for Medicare & Medicaid Services (CMS) proposes that the evidence is insufficient to conclude that the use of positron emission tomography (PET) amyloid-beta (Aβ) imaging improves health outcomes for Medicare beneficiaries with dementia or neurodegenerative disease, and thus PET Aβ imaging is not reasonable and necessary.

CMS does not currently cover PET Aβ imaging. In July 2012, Lilly USA LLC, the manufacturer of the PET amyloid radiopharmaceutical florbetapir (Amyvid), requested that CMS reconsider its non-coverage decision for PET scans and provide coverage for the use of PET amyloid imaging as a diagnostic test to “estimate amyloid neuritic plaque density in adult patients with documented cognitive impairment who are being evaluated for Alzheimer’s disease (AD) and other causes of cognitive impairment.” However, the agency states that there is sufficient evidence that the use of PET Aβ imaging could be promising in two scenarios:

1. To exclude AD in narrowly defined and clinically difficult differential diagnoses, such as AD versus frontotemporal dementia (FTD).
2. To enrich clinical trials seeking better treatments or prevention strategies for AD by allowing for selection of patients on the basis of biological as well as clinical and epidemiological factors.

Therefore, CMS proposes to cover one PET Aβ scan per patient through coverage with evidence development (CED) in clinical studies with the following objectives:

- To develop better treatments or prevention strategies for AD, or, as a strategy to identify subpopulations at risk for developing AD.
- To resolve clinically difficult differential diagnoses (e.g., FTD versus AD) where the use of PET Aβ
imaging appears to improve health outcomes.

Clinical studies must be approved by CMS, involve subjects from appropriate populations; be comparative, prospective and longitudinal; and use randomization and postmortem diagnosis as the endpoint where appropriate. Radiopharmaceuticals used in the PET Aβ scans must be FDA approved and the studies must address one or more of the following questions:

1. Do the results of PET Aβ imaging lead to improved health outcomes? Meaningful health outcomes of interest include: avoidance of futile treatment or tests; improving, or slowing, the decline of quality of life; and survival.
2. Are there specific subpopulations, patient characteristics, or differential diagnoses that are predictive of improved health outcomes in patients whose management is guided by PET Aβ imaging?
3. Does using PET Aβ imaging in guiding patient management, to enrich clinical trials seeking better treatments or prevention strategies for AD by selecting patients on the basis of biological as well as clinical and epidemiological factors, lead to improved health outcomes?

National Coverage Determination (NCD) for FDG PET for Dementia and Neurodegenerative Diseases (220.6.13) states: Medicare covers FDG Positron Emission Tomography (PET) scans for either the differential diagnosis of fronto-temporal dementia (FTD) and Alzheimer’s disease (AD) under specific requirements; OR, its use in a Centers for Medicare & Medicaid Services (CMS)-approved practical clinical trial focused on the utility of FDG PET in the diagnosis or treatment of dementing neurodegenerative diseases.

An FDG PET scan is considered reasonable and necessary in patients with a recent diagnosis of dementia and documented cognitive decline of at least 6 months, who meet diagnostic criteria for both AD and FTD. These patients have been evaluated for specific alternate neurodegenerative diseases or other causative factors, but the cause of the clinical symptoms remains uncertain.

The following additional conditions must be met before an FDG PET scan will be covered:

a. The patient’s onset, clinical presentation, or course of cognitive impairment is such that FTD is suspected as an alternative neurodegenerative cause of the cognitive decline. Specifically, symptoms such as social disinhibition, awkwardness, difficulties with language, or loss of executive function are more prominent early in the course of FTD than the memory loss typical of AD;

b. The patient has had a comprehensive clinical evaluation (as defined by the American Academy of Neurology encompassing a medical history from the patient and a well-acquainted informant (including assessment of activities of daily living), physical and mental status examination (including formal documentation of cognitive decline occurring over at least 6 months) aided by cognitive scales or neuropsychological testing, laboratory tests, and structural imaging such as magnetic resonance imaging (MRI) or computed tomography (CT);

c. The evaluation of the patient has been conducted by a physician experienced in the diagnosis and assessment of dementia;

d. The evaluation of the patient did not clearly determine a specific neurodegenerative disease or other cause for the clinical symptoms, and information available through FDG PET is reasonably expected to help clarify the diagnosis between FTD and AD and help guide future treatment;
e. The FDG PET scan is performed in a facility that has all the accreditation necessary to operate nuclear medicine equipment. The reading of the scan should be done by an expert in nuclear medicine, radiology, neurology, or psychiatry, with experience interpreting such scans in the presence of dementia;

f. A brain single photon emission computed tomography (SPECT) or FDG PET scan has not been obtained for the same indication. (The indication can be considered to be different in patients who exhibit important changes in scope or severity of cognitive decline, and meet all other qualifying criteria listed above and below (including the judgment that the likely diagnosis remains uncertain.) The results of a prior SPECT or FDG PET scan must have been inconclusive or, in the case of SPECT, difficult to interpret due to immature or inadequate technology. In these instances, an FDG PET scan may be covered after one year has passed from the time the first SPECT or FDG PET scan was performed.)

g. The referring and billing provider(s) have documented the appropriate evaluation of the Medicare beneficiary. Providers should establish the medical necessity of an FDG PET scan by ensuring that the following information has been collected and is maintained in the beneficiary medical record:
   i. Date of onset of symptoms;
   ii. Diagnosis of clinical syndrome (normal aging; mild cognitive impairment (MCI); mild, moderate or severe dementia);
   iii. Mini mental status exam (MMSE) or similar test score;
   iv. Presumptive cause (possible, probable, uncertain AD);
   v. Any neuropsychological testing performed;
   vi. Results of any structural imaging (MRI or CT) performed;
   vii. Relevant laboratory tests (B12, thyroid hormone); and,
   viii. Number and name of prescribed medications.

CMS has not established a National Coverage Determination (NCD) for the use of PET for autism spectrum disorders (ASDs).

3. MINNESOTA DEPARTMENT OF HUMAN SERVICES (DHS):
To be eligible for MHCP payment for radiology, the service must:
• Be ordered and provided by or under the direction of a recipient’s treating physician (MD, DO, DPM, DDS, Chiropractor) or practitioner (nurse practitioner, clinical nurse specialist, physician assistant or certified professional midwife), within the scope of practice as defined by state law, who furnished a consultation or treats a recipient for a specific medical problem,
• Yield results that must be used by the treating physician or practitioner in screening, diagnosis or management of a recipient’s specific health problem,
• Meet Medicare or DHS coverage criteria (DHS 2014.)

CLINICAL EVIDENCE:
Findings from 5 studies found stand-alone PET moderately to highly specific (84% to 100%) for detecting regional lymph node melanoma metastasis when compared with histology results from SLNB with or
without conventional imaging; however, sensitivity was very low (8% to 22%). Findings from 9 studies indicate that for distant metastasis compared to histology with or without conventional imaging PET was associated with a specificity of 86% to 100%. Corresponding sensitivity values were 79% to 94% in 6 studies and 0% and 40% in 3 studies. Evidence from 1 of these studies suggests that the sensitivity of PET varied markedly depending on lesion size. The other 2 studies enrolled only patients with early-stage melanoma and so were unlikely to have distant metastasis.

A number of small to very small prospective case series studies evaluating PET in patients with suspected or known prostate cancer were identified in the literature. The majority of studies that used PET for diagnosis or staging provided histological confirmation of PET findings, while those that utilized PET for detection of bone metastases reported bone scan findings as the criterion standard. Most of the studies assessed 18F-FDG PET, although there were several studies that examined the utility of the radiotracer 11C-choline for diagnosis, staging, and restaging. In one study each, 11C-putrescine PET was used for staging and restaging, and 11C-5-hydroxytryptophan was used for restaging. None of the studies addressed the question of how the use of PET might impact patient management or provided evidence regarding the effect of PET on disease outcome or survival. The findings of all of the reviewed studies are summarized in the following sections, and the data from these studies are provided in Table 3. Since 18F-FDG was most commonly used as the PET radiotracer, values derived for the accuracy of 18F-FDG PET are repeated in Table 4 to assist in interstudy comparison.

For localizing seizure focus, 18F-FDG PET demonstrated a sensitivity of 36% to 100% (mean, 73%; median, 78%), a false-localization rate of 0% to 33% (mean, 8%; median, 7%), a no-localization rate of 0% to 57% (mean, 18%; median, 20%), and a positive predictive value of 64% to 100% (mean, 89%; median, 92%) in 12 studies. In six studies, 11C-FMZ PET with quantitative analysis demonstrated a sensitivity of 69% to 100% (mean, 93%; median, 100%), a false-localization rate of 0% (mean and median, 0%), a no-localization rate of 0% to 31% (mean, 6%; median, 0%), and a positive predictive value of 93% to 100% (mean, 99%; median, 100%). In five studies examining PET for functional brain mapping, all involved activation 15O-H2O PET for lateralizing/localizing eloquent cortex for language, used a variety of activation tasks and quantitative analysis protocols, and failed to specify blinding status. Histopathologic data and surgical outcome were available in three studies in 50% to 100% of the cases.

Overall, it appears that 82Rb or 13NH3 PET MPI may be relatively accurate and comparable with or superior to most other noninvasive tests for evaluating CAD. Despite this, no data are available to show the potential impact of these PET protocols on treatment decisions or health outcome. The high cost of PET and the relatively high accuracy of SPECT suggest that PET may not be used often for evaluating CAD. However, it may be warranted for this purpose in patients for whom SPECT is unavailable, inconclusive, or associated with the potential for attenuation problems or other technical difficulties or patients for whom angiography is associated with high risk for morbidity or technical challenge.

Available studies indicate that PET may be useful for disorders associated with dementia or impaired movement, including Alzheimer's disease (AD), Huntington's disease (HD), Wilson's disease (WD), and Parkinson's disease (PD). In addition to diagnosis, these applications include assessing response to therapy and improved knowledge of disease mechanisms for AD, HD, WD, and PD, which potentially may lead to improved management of all four disorders; early identification of presymptomatic metabolic changes in AD, which may potentially prevent excessive loss of brain tissue through earlier initiation of treatment; and determining the appropriate site(s) for fetal tissue implants in PD, which may potentially result in improved outcome for this intervention. For these applications, a variety of radiotracers have been used, including,
but not limited to: $^{82}\text{Rb}$ or $^{13}\text{NH}_3$, $^{18}\text{F-FDG}$, $^{15}\text{O-H}_2\text{O}$, $^{11}\text{C-MP4A}$, $^{11}\text{C-PIB}$, $^{18}\text{F-FDDNP}$, $^{11}\text{C-DTBZ}$, $^{11}\text{C-FMZ}$.

Four studies compared cerebral metabolic rates in patients with autism and controls at rest (Rumsey et al., 1985, Heh et al., 1989, Buchsbaum et al., 1992, Zilbovicius et al., 2000), while three studies assessed metabolic rates and functional changes during perception and learning (Müller et al., 1999, Haznedar et al., 2000, Hall et al., 2003), and one study assessed dopaminergic function (Fernell et al., 1997). The studies focused on a variety of factors and provided conflicting results.

**SUMMARY:**

The evidence is adequate to determine that the results of FDG PET imaging are useful in determining the appropriate anti-tumor treatment strategy to improve health outcomes.

Based on evidence published in the last 10 years for patients with known or suspected metastatic melanoma, the findings for positron emission tomography (PET) are mixed. When used in conjunction with other imaging modalities, PET is highly specific and moderately sensitive in detecting distant metastasis in patients already identified as having or suspected of having metastatic melanoma.

Based on evidence from a small number of studies reporting high specificity but low sensitivity, it appears that PET does not add value to staging of patients with metastatic disease limited to the regional lymph nodes.

The use of PET scanning in the diagnosis and staging of prostate cancer is hampered by the generally low metabolic activity of most prostate tumors and their metastases. It has shown promise for staging and restaging persons with advanced-stage disease and aggressive tumors suspected by a high tumor grade and high prostate-specific antigen velocity. Further investigations are needed to ascertain the eventual place of PET scans in prostate cancer.

There is evidence to support the use of $^{18}\text{F-FDG}$ PET for lateralizing or localizing seizure focus in the preoperative evaluation of medically refractory epilepsy when surface EEG techniques reveal focal, unilateral abnormality and findings from MRI are negative, nondiagnostic, equivocal, or discordant with surface EEG.

Overall, in the use of PET for lateralizing and localizing seizure focus, it appears that $^{18}\text{F-FDG}$ PET with standard visual, semiquantitative, or quantitative analysis methods and $^{11}\text{C-FMZ}$ PET with quantitative analysis may be relatively reliable and at least comparable with most other noninvasive modalities.

For functional brain mapping, PET may have the potential for obviating invasive tests for language lateralization, thereby altering disease management and reducing costs. However, no data are available to confirm this or to address the impact of PET language mapping on health outcome. Further study is needed to assess $^{15}\text{O-H}_2\text{O}$ PET with visual and semiquantitative analysis or alternative language activation tasks and to assess PET for brain mapping of functions other than language.

Only four studies could be found regarding the use of PET for assessing treatment of epilepsy. Additional study is required to verify the efficacy, benefit, and role of PET in this capacity. No data are available regarding the comparative performance of PET with other modalities, the impact of PET on disease management or health outcome, or the cost-effectiveness of PET.

In Alzheimer’s disease patients, $^{18}\text{F-FDG}$ PET demonstrated significant hypometabolism in temporal and/or parietal regions and, often, posterior cingulate, frontal, and/or other regions, compared with controls. The
areas of hypometabolism reflected areas known to involve pathologic changes in AD. $^{18}$F-FDG PET also revealed differences in the pattern of hypometabolism or in the degree of regional hypometabolism between AD and DLB, FTD/FTLD, VaD, or MCI. However, the pattern and degree of hypometabolism in AD patients varied, frequently resembled that of other dementias, and appeared to be influenced by the severity of dementia, the age at AD onset, the presence and dose of APOE E4, the duration between $^{18}$F-FDG injection and scanning, and the method used for analyzing PET data. Despite this, $^{18}$F-FDG PET achieved relatively high accuracy in diagnosing AD, even in patients with questionable or mild dementia. Dubroff and Nasrallah (2015) confirm that amyloid PET imaging demonstrates high sensitivity for pathologic cerebral amyloid deposition in multiple studies. However, they also note principal drawbacks to this new diagnostic test, such as declining specificity in older age groups and an uncertain clinical role given the lack of available treatments that would change to course of AD.

Overall, there are few studies using PET in autistic patients, and the focus of the studies has varied widely. Therefore, no strong conclusions can be drawn from the study results so far.

**APPLICABLE CODES:**

The Current Procedural Terminology (CPT®) codes and HCPCS codes listed in this policy are for reference purposes only. Listing of a service or device code in this policy does not imply that the service described by this code is a covered or non-covered health service. The inclusion of a code does not imply any right to reimbursement or guarantee claims payment. Other medical policies and coverage determination guidelines may apply.

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<tr>
<th>HCPCS Codes</th>
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<tbody>
<tr>
<td>A9552</td>
<td>Fluorodeoxyglucose F-18 FDG, diagnostic, per study dose, up to 45 millicuries</td>
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<tr>
<td>G0219</td>
<td>PET imaging whole body; melanoma for non-covered indications</td>
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<tr>
<td>G0235</td>
<td>PET imaging, any site, not otherwise specified</td>
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<tr>
<td>G0252</td>
<td>PET imaging, full and partial-ring PET scanners only, for initial diagnosis of breast cancer and/or surgical planning for breast cancer (e.g., initial staging of axillary lymph nodes)</td>
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<td>Malignant melanoma of skin</td>
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<tr>
<td>299.0</td>
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<td>294.8</td>
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<td>G3183</td>
<td>Dementia with Lewy bodies</td>
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<td>G3184</td>
<td>MCI, so stated</td>
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<td>G3189</td>
<td>Other specified degenerative diseases of nervous system</td>
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Clinical & Quality Management MEDICAL POLICY

G319 Degenerative disease of nervous system, unspecified
Z80.8 Family history of malignant neoplasm of other organs or systems
Z85.820 Personal history of malignant melanoma of skin

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<td>Myocardial imaging, positron emission tomography (PET), metabolic evaluation</td>
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<td>Myocardial imaging, positron emission tomography (PET), perfusion; multiple studies at rest and/or stress</td>
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<td>78608</td>
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<td>Tumor imaging, positron emission tomography (PET); skull base to mid-thigh</td>
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<td>Tumor imaging, positron emission tomography (PET); whole body</td>
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<td>78814</td>
<td>Tumor imaging, positron emission tomography (PET) with concurrently acquired CT for attenuation correction and anatomical localization; limited area (e.g., chest, head/neck)</td>
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REFERENCES:


75. Vees H, Buchegger F, Albrecht S, et al. 18F-choline and/or 11C-acetate positron emission tomography: detection of residual or progressive subclinical disease at very low prostate-specific antigen values (<1 ng/mL) after radical prostatectomy. BJU Int. 2007;99(6):1415-1420.


POLICY HISTORY:

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