MEDICAL POLICY

MEDICAL POLICY DETAILS	
Medical Policy Title	**Positron Emission Tomography (PET) - Non-Oncologic Applications**
Policy Number	**6.01.07**
Category	**Technology Assessment**
Original Effective Date	**10/18/01**
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Archive Review Date	**N/A**
Product Disclaimer	• *If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.* • *If a commercial product (including an Essential Plan or Child Health Plus product), medical policy criteria apply to the benefit.* • *If a Medicaid product covers a specific service, and there are no New York State Medicaid guidelines (eMedNY) criteria, medical policy criteria apply to the benefit.* • *If a Medicare product (including Medicare HMO-Dual Special Needs Program (DSNP) product) covers a specific service, and there is no national or local Medicare coverage decision for the service, medical policy criteria apply to the benefit.* • *If a Medicare HMO-Dual Special Needs Program (DSNP) product DOES NOT cover a specific service please refer to the Medicaid Product coverage line.*

POLICY STATEMENT

I. Based upon our criteria and assessment of the peer-reviewed literature, fluorodeoxyglucose (FDG) positron emission tomography (PET) using a full ring dedicated PET scanner is considered **medically appropriate** for the following indications:

A. Epileptic Seizures:
1. Seizure disorders with failed response to medical therapy when being considered for resection of suspected epileptogenic focus in a region of the brain accessible by surgery.

B. To differentiate Alzheimer's disease (AD) from frontotemporal lobe dementia (FTLD) in patients with a recent diagnosis of dementia, when **ALL** of the following are present:
1. Patient meets diagnostic criteria for AD and FTLD;
2. Patient has a documented cognitive decline of at least six months' duration;
3. Evaluation has ruled out specific alternative neurodegenerative diseases or causative factors;
4. Cause of clinical symptoms is uncertain; and
5. Results are expected to help clarify the diagnosis between FTLD and AD and help guide future treatment.

C. To evaluate patients suspected of having encephalitis, including autoimmune encephalitis, if diagnosis remains unclear after evaluation with brain magnetic resonance imaging (MRI), cerebrospinal fluid (CSF) analysis, and lab testing, including serology, if appropriate.

II. Based upon our criteria and assessment of the peer-reviewed literature, the use of beta amyloid PET imaging using amyloid specific tracers (e.g., Amyvid, Vizamyl, Neuraceq) for the diagnosis of Alzheimer's Disease and differentiating between Alzheimer's disease and other neurodegenerative/neurologic disorders has not been medically proven to be effective and, therefore, is considered **investigational**.

III. Based upon our criteria and assessment of the peer-reviewed literature, the use of PET scanning has not been medically proven to be effective and, therefore, is considered **investigational** for all other indications, including but not limited to:
   A. Anorexia nervosa;
   B. Auto-immune disorders with central nervous system (CNS) manifestations, including Behcets' syndrome and lupus erythematosus;
   C. Cerebral blood flow in newborns (vegetative versus locked-in syndrome);
   D. Cerebrovascular diseases, including arterial occlusive disease (arteriosclerosis, atherosclerosis), carotid artery disease, cerebral aneurysm, arteriovenous malformation (AVM) hemorrhage, infarct, and ischemia;
   E. Chronic fatigue syndrome (CFS);
   F. Degenerative motor neuron diseases, including amyotrophic lateral sclerosis (ALS), Friedreich's ataxia, olivopontocerebellar atrophy, Parkinson's disease, progressive supranuclear palsy, Shy-Drager syndrome, spinocerebellar degeneration, Steele-Richardson-Olszewski disease, and Tourette's syndrome;
   G. Dementias, including dementia with Lewy-bodies, multi-infarct dementia, chronic traumatic encephalopathy, normal pressure hydrocephalus, Pick's disease, presenile dementia, Alzheimer's disease, and frontotemporal dementia, except as listed in Policy Statement I.B.;
   H. Demyelinating diseases, such as multiple sclerosis;
   I. Developmental, congenital, or inherited disorders, including adrenoleukodystrophy, autism spectrum disorders, Down's syndrome, Huntington Chorea, kinky-hair disease (Menkes' syndrome), Sturge-Weber syndrome (encephalofacial angiomatosis), and the phakomatoses;
   J. Diagnosis and non-surgical treatment of epilepsy and convulsive disorders;
   K. Fever of unknown origin, infectious process;
   L. Giant cell arteritis;
   M. Inflammatory bowel disease;
   N. Inflammation of unknown origin;
   O. Joint replacement follow-up;
   P. Migraines;
   Q. Mycobacterium infection;
   R. Nutritional or metabolic diseases and disorders, including acanthocytes, hepatic encephalopathy, hepatolenticular degeneration, metachromatic leukodystrophy, mitochondrial disease, and subacute necrotizing encephalomyelopathy;
   S. Post-traumatic stress disorder;
   T. Psychiatric disease and disorders, including affective disorders, depression, obsessive-compulsive disorder, psychomotor disorders, and schizophrenia;
   U. Pulmonary diseases, including adult respiratory distress syndrome, diffuse panbronchiolitis, emphysema, obstructive lung disease, and pneumonia;
   V. Pyogenic infections, including aspergillosis and encephalitis;
   W. Sarcoidosis (cardiac sarcoid - please refer to *Corporate Medical Policy #6.01.41 Positron Emission Tomography (PET)-Cardiac Applications*);
   X. Sick building syndrome;
   Y. Spondylodiscitis;
   Z. Substance use disorder, including CNS effects of alcohol, cocaine, and heroin;
   AA. Trauma, including brain injury and carbon monoxide poisoning;
   BB. Vasculitis; and
   CC. Viral infections, including acquired immune deficiency syndrome (AIDS), AIDS dementia complex, Creutzfeldt-Jakob syndrome, progressive multifocal leukoencephalopathy, progressive rubella encephalopathy, and subacute sclerosing panencephalitis.

Refer to Corporate Medical Policy #6.01.29 Positron Emission Tomography (PET)-Oncologic Applications.

Refer to Corporate Medical Policy #6.01.41 Positron Emission Tomography (PET)-Cardiac Application

Refer to Corporate Medical Policy #11.01.03 Experimental or Investigational Services.

DESCRIPTION

PET scanning is an imaging technology that can reveal metabolic information in various tissue sites. The metabolic information is what distinguishes it from other imaging modalities, such as magnetic resonance imaging (MRI) and computed tomography (CT), which provide primarily anatomic information. PET scans measure concentrations of radioactive chemicals that are partially metabolized in the body. PET scans are based on the use of positron emitting radionuclide tracers coupled to organic molecules such as glucose, ammonia, or water. Dedicated PET scanners consist of multiple detectors arranged in a full or partial ring around the patient.

A variety of radiotracers are used for PET scanning, including fluorine-18, rubidium-82, ammonia N-13, carbon-11, oxygen-15, and nitrogen-13. Fluorine-18 is often coupled with FDG as a means of detecting glucose metabolism, which, in turn, reflects the metabolic activity, and, thus, viability, of the target tissue. Because of their short half-life, tracers must be made locally. With the exception of fluorine and rubidium, all the tracers must be manufactured with an on-site cyclotron.

Florbetapir (Amyvid, Avid Radiopharmaceuticals), a radioactive dye for visualization of amyloid plaque in the brain, was approved by the United States Food and Drug Administration (FDA) in 2012. The FDA document prepared for the approval process indicated that, while florbetapir may detect pathology, there could be no claim of disease detection, as beta amyloid aggregates can be found in cognitively normal elderly individuals, as well as patients with AD. Amyvid is indicated for PET imaging of the brain, to estimate beta-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for AD and other causes of cognitive decline. A second radioactive dye, Flutemetamol F18 injection (Vizamyl, GE Healthcare), was approved by the FDA in October 2013. Flutemetamol F18 is not indicated to predict the development of AD or to check how patients respond to treatment for AD. Flutemetamol F18 PET images should be interpreted only by health care professionals who successfully complete training in an image interpretation program. In March 2014, the FDA approved a third radioactive dye, Florbetaben F18 (Neuraceq, Piramal Life Sciences, Matran, Switzerland).

RATIONALE

The FDA has approved the scanner and imaging hardware for PET as being substantially equivalent to x-ray CT . The FDA requires submission of a new drug application (NDA) for approval of PET radiotracers. Because PET radiotracers have an extremely short half-life, they must be produced in the clinical setting. The FDA also regulates drug manufacturing processes in PET facilities. In 1991, the FDA approved the use of Rubidium 82 (Rb 82) as a myocardial perfusion tracer and, in 1999, approved the use of ammonia N-13 as a myocardial perfusion tracer.

Clinical evidence supports that the use of Rubidium 82 (Rb-82) PET and ammonia N-13 PET scans in clinical practice has the potential to improve net health outcomes through changes in patient management. Studies demonstrate that both tracers have high reliability and validity in the evaluation of myocardial perfusion.

Clinical evidence is inadequate to support the use of FDG PET scanning for routine use in the diagnostic evaluation of dementia. Although FDG PET scanning appears to have promise for use as an adjunct to clinical diagnosis of AD, further prospective studies are needed to establish the value that it brings to diagnosis over and above a competent clinical diagnosis. The Alzheimer's Disease Neuroimaging Initiative (ADNI), a longitudinal, five-year, prospective trial sponsored by the National Institute on Aging, included 800 participants aged 55 to 90 years (400 with mild cognitive impairment, 200 with AD, 200 with no known cognitive impairment) who were followed for two years. At 58 sites in the U.S. and Canada, ADNI compared neuroimaging (PET and MRI), biological, and clinical information. It sought correlations among data to track the progression of memory loss from its earliest stages, and also identify critical markers that responded to treatments aimed at slowing progression of mild cognitive impairment and AD. Enrollment began in early 2006 and the clinical trial end date was October 2009.

With the development of the following PET scan radiotracers PiB (Pittsburgh Compound B), Florbetapir F18 (Amyvid), Flutemetamol F18 injection (Vizamyl), and Florbetaben F18 (Neuraceq) as well as newly identified radiotracers, the detection of β amyloid deposits in the brain is possible. Studying β amyloid positivity/negativity in healthy older adults, older adults with mild cognitive impairment and in adults diagnosed with AD is an active area of research especially as more of the aging population becomes afflicted with AD.

Clinical evidence in the form of small prospective and retrospective studies totaling 166 patients, and a meta-analysis of 19 studies, support that FDG PET is highly accurate in diagnosing chronic osteomyelitis.

Several studies with methodologic flaws indicate that there are instances in which PET may be helpful in the diagnosis of fever of unknown origin and infection. However, clinical evidence is not sufficient to consider these indications medically appropriate.

FDG PET has been investigated for potential use in the diagnosis and follow-up of giant cell arteritis. Clinical evidence consists of small case series, retrospective studies, and case reports. Although some reports consider PET promising for this indication, results need to be confirmed in larger, prospective studies. The limited spatial resolution of PET scanners is a technical limitation that prevents the detection of metabolic signals within anatomical structures smaller than four to five millimeters in size. In addition, the physiological uptake of FDG by the grey matter of the brain obscures FDG uptake within the temporal arteries.

CODES

- *Eligibility for reimbursement is based upon the benefits set forth in the member's subscriber contract.*
- *CODES MAY NOT BE COVERED UNDER ALL CIRCUMSTANCES. PLEASE READ THE POLICY AND GUIDELINES STATEMENTS CAREFULLY.*
- *Codes may not be all inclusive as the AMA and CMS code updates may occur more frequently than policy updates.*

CPT Codes

Code	Description
78608	Brain imaging, positron emission tomography, (PET); metabolic evaluation
78609	perfusion evaluation
78811	Positron emission tomography (PET) imaging; limited area (e.g., chest, head/neck)
78812	skull base to mid-thigh
78813	whole body
78814	Positron emission tomography (PET) with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization imaging; limited area (e.g. chest, head/neck)
78815	skull base to mid-thigh
78816	whole body

HCPCS Codes

Code	Description
A9526	Nitrogen N-13 ammonia, diagnostic, per study dose, up to 40 millicuries
A9552	Fluorodeoxyglucose F-18 FDG, diagnostic, per study dose, up to 45 millicuries
A9555	Rubidium Rb-82, diagnostic, per study dose, up to 60 millicuries

Code	Description
A9586 **(E/I)**	Florbetapir F18, diagnostic, per study dose, up to 10 millicuries
A9598 **(E/I)**	Positron emission tomography radiopharmaceutical, diagnostic, for non-tumor identification, not otherwise classified
A9601 **(E/I)**	Flortaucipir f 18 injection, diagnostic, 1 millicurie (Effective 07/01/2022)
A9602 **(E/I)**	Fluorodopa f-18, diagnostic, per millicurie (Effective 10/01/2022)
Q9982 **(E/I)**	Flutemetamol F18, diagnostic, per study dose, up to 5 millicuries
Q9983 **(E/I)**	Florbetaben F18, diagnostic, per study dose, up to 8.1 millicuries
S8085 **(E/I)**	Fluorine-18 fluorodeoxyglucose (F-18 FDG) imaging using dual-head coincidence detection system (non-dedicated PET scan)

ICD10 Codes

Code	Description
D33.0-D33.9	Benign neoplasm of brain and other parts of central nervous system (code range)
D43.0-D43.9	Neoplasm of uncertain behavior of brain and central nervous system (code range)
D49.6	Neoplasm of unspecified behavior of brain
F01.50-F03.91	Dementia due to known physiological conditions (code range)
G30.0-G30.9	Alzheimer Disease (code range)
G40.001-G40.219	Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset (code range)
G40.301-G40.319	Generalized idiopathic epilepsy and epileptic syndromes (code range)
G40.901-G40.919	Epilepsy, unspecified (code range)

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*Key Article

KEY WORDS

FDG PET, FDG SPECT, Gamma Camera, Ammonia N-13, Rubidium 82, Florbetapir F18, Flutemetamol F18, Florbetaben F18, and Fluorine-18 fluorodeoxyglucose.

CMS COVERAGE FOR MEDICARE PRODUCT MEMBERS

There is currently a National Coverage Determination (NCD) for PET scans. Please refer to the following NCD website for Medicare Members: http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=211&ncdver=4&bc=AgAAgAAAAAAA&

There is currently a National Coverage Determination (NCD) for FDG PET for Dementia and Neurodegenerative Diseases. Please refer to the following NCD website for Medicare Members: http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=288&ncdver=3&bc=BAABAAAAAAAA&

There is currently a National Coverage Determination (NCD) for Beta Amyloid Positron Tomography in Dementia and Neurodegenerative Disease. Please refer to the following NCD website for Medicare Members:

http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=356&ncdver=1&bc=AgAAgAAAAAAAAA%3d%3d&