

MEDICAL POLICY



SUBJECT: POSITRON EMISSION TOMOGRAPHY (PET) NON-ONCOLOGIC APPLICATIONS	EFFECTIVE DATE: 11/18/99 REVISED DATE: 04/19/00, 04/19/01, 01/17/02, 10/16/02, 01/16/03, 10/15/03, 10/20/04, 10/20/05, 11/16/06, 08/16/07, 08/21/08, 09/17/09, 12/16/10, 01/20/11, 12/15/11, 01/17/13, 05/22/14, 02/19/15, 02/18/16, 02/16/17, 02/15/18
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<ul style="list-style-type: none">• <i>If a product excludes coverage for a service, it is not covered, and medical policy criteria do not apply.</i>• <i>If a commercial product, including an Essential Plan product, covers a specific service, medical policy criteria apply to the benefit.</i>• <i>If a Medicare 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.</i>	

POLICY STATEMENT:

- I. Based upon our criteria and assessment of peer reviewed literature, 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.
 2. When conventional techniques for seizure localization provide data that suggests a seizure focus but are not sufficiently conclusive to permit surgery.
 - B. Movement disorders:
 1. Suspected Huntington's chorea when MRI is non diagnostic and genetic testing is inconclusive; or
 2. Progressive ataxia of undetermined etiology.
 - D. Chronic osteomyelitis when bone scan and/or MRI is non-diagnostic.
 - E. To differentiate Alzheimer's disease (AD) from frontotemporal lobe dementia (FTLD) in patients with a recent diagnosis of dementia and all of the following:
 1. Meets diagnostic criteria for AD and FTLD; and
 2. Has a documented cognitive decline of at least 6 months; and
 3. Evaluation has ruled out specific alternative neurodegenerative diseases or causative factors; and
 4. Cause of clinical symptoms is uncertain; and
 5. The results are expected to help clarify the diagnosis between FTLD and AD and help guide future treatment.
- 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™, Vizamyil™, Neuraceq™) for dementia has not been medically proven to be effective and 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 is considered **investigational** for all other indications, including, but not limited to:
 - A. Anorexia Nervosa;
 - B. Auto-immune disorders with CNS manifestations, including Behcets' syndrome, lupus erythematosus;
 - D. Cerebral blood flow in newborns;
 - E. Cerebrovascular diseases, including arterial occlusive disease (arteriosclerosis, atherosclerosis), carotid artery disease, cerebral aneurysm, cerebrovascular malformations (AVM) hemorrhage, infarct, ischemia;
 - F. Chronic fatigue syndrome;
 - G. 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, Tourette's syndrome;
 - H. Dementias, including, dementia with Lewy-bodies, multi-infarct dementia, Pick's disease, presenile dementia, Alzheimer's disease, and frontotemporal dementia except as listed in Policy Statement IE;

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- I. Demyelinating diseases, such as multiple sclerosis;
- J. Developmental, congenital, or inherited disorders, including adrenoleukodystrophy, Down's syndrome, Kinky-hair disease (Menkes' syndrome), Sturge-Weber syndrome (encephalofacial angiomas), 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, 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 regarding Positron Emission Tomography (PET) Cardiac Applications)
- X. Sick building syndrome;
- Y. Spondylodiscitis;
- Z. Substance abuse, including CNS effects of alcohol, cocaine, and heroin;
- AA. Trauma, including brain injury and carbon monoxide poisoning;
- BB. Vasculitis;
- 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 regarding Positron Emission Tomography-Oncologic Applications.

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

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

POLICY GUIDELINES:

The Federal Employees Health Benefit Program (FEHBP/FEP) requires that procedures, devices or laboratory tests approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational and thus these procedures, devices or laboratory tests may be assessed only on the basis of their medical necessity.

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DESCRIPTION:

Positron emission tomography (PET) 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) that provide primarily anatomic information. PET scans measure concentrations of radioactive chemicals that are partially metabolized in the body and 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 fluoro-deoxyglucose (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 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 FDA in 2012. The FDA document prepared for the advisory committee meeting indicated that while florbetapir may detect pathology, there could be no claim of disease detection, since beta amyloid aggregates can be found in cognitively normal elderly individuals, as well as patients with AD. Amyvid™ is indicated for PET (positron emission tomography) imaging of the brain to estimate beta-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer’s disease 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 U.S. Food and Drug Administration (FDA) has approved the scanner and imaging hardware for PET as being substantially equivalent to x-ray computed tomography (CT). The FDA requires PET radiotracers to be approved through a new drug approval (NDA) process. Because PET radiotracers have an extremely short half-life, they must be produced in the clinical setting. The FDA also intends to regulate 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 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 Alzheimer’s disease, further prospective studies are needed to establish the value that it brings to diagnosis over and above a competent clinical diagnosis. A National Institute on Aging longitudinal, five-year, prospective trial, the Alzheimer’s Disease Neuroimaging Initiative (ADNI), plans to include 800 participants aged 55-90 years (400 with mild cognitive impairment, 200 with Alzheimer’s disease, 200 normal participants) to be followed for two years. At 58 sites in the U.S. and Canada ADNI will compare neuroimaging (PET and MRI), biological, and clinical information. It will seek correlations among data that will track the progression of memory loss from its earliest stages, and identify critical markers that response to treatments aimed at slowing progression of mild cognitive impairment and Alzheimer’s disease. Enrollment began in early 2006 and the end date is anticipated to be October 2009.

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A 2013 BlueCross BlueShield Technical Assessment concluded that beta amyloid imaging with positron emission tomography (PET) to evaluate suspected Alzheimer’s disease (AD) and other causes of cognitive decline does not meet the TEC criteria, based on the lack of direct evidence for clinical utility. The test is not likely to be useful for confirming AD in patients who present with cognitive impairment. It may have a role in ruling out Alzheimer’s disease (AD), but this has yet to be established with certainty. Questions also remain about the use of this test outside of the investigational setting, particularly regarding the accuracy of visual interpretation of images and how best to apply this test in routine clinical practice.

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 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 4-5 mm in size. In addition, the physiological uptake of FDG by the grey matter of the brain obscures FDG uptake within the temporal arteries.

CODES: Number Description

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.

Code Key: Experimental/Investigational = (E/I), Not medically necessary/ appropriate = (NMN).

<u>CPT:</u>	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) imaging with concurrently acquired computed tomography (CT) for attenuation correction and anatomical localization; limited area (e.g. chest, head/neck)
	78815	skull base to mid-thigh
	78816	whole body

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<u>HCPCS:</u>	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

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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
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:	
D33.0-D33.2	Benign neoplasm of brain and other parts of central nervous system (code range)
D43.0-D43.4	Neoplasm of uncertain behavior of brain and spinal cord (code range)
D49.6	Neoplasm of unspecified behavior of brain
G40.001-G40.219	Localization-related (focal) (partial) idiopathic epilepsy and epileptic syndromes with seizures of localized onset (code range)
G40.301-G40.3119	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.

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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=BAABAAAAAAA&>

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=AgAAgAAAAAAA%3d%3d&>