

<b>Title</b>	<b>Cardiac Applications of PET Scanning</b>
<b>Number</b>	<b>CP.MP.BC.6.01.20*</b>
<b>Revision Date(s)</b>	09/12/06; 03/08/05; 05/11/04; 03/11/03; 09/21/00; 06/01/99
<b>Effective Date</b>	September 12, 2006
<b>Replaces</b>	N/A
<b>Cross References</b>	<a href="#">CP.MP.BC.6.01.06 Miscellaneous Applications of Positron Emission Tomography (PET)</a> <a href="#">CP.MP.AR.6.01.27 FDG Using Camera-Based Imaging (FDG-SPECT)</a> <a href="#">CP.MP.PR.6.01.505 Oncologic Applications of PET Scanning</a>

<b>Description</b>	<p>Positron emission tomography (PET) scans are based on the use of positron-emitting radionuclide tracers, which simultaneously emit two high energy photons in opposite directions. These photons can be simultaneously detected (referred to as coincidence detection) by a PET scanner, consisting of multiple stationary detectors that encircle the thorax. Compared to SPECT scans (single photon emission computed tomography), coincidence detection offers greater spatial resolution.</p> <p>A variety of tracers are used for PET scanning, including fluorine-18, rubidium-82, oxygen-15, nitrogen-13, and carbon-11. 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. The tracers may be coupled to a variety of physiologically active molecules. For example, fluorine-18 is often coupled with fluorodeoxyglucose as a means of detecting glucose metabolism, which in turn reflects the metabolic activity, and thus the viability, of the target tissue.</p> <p>In terms of cardiac applications, PET scanning has focused on two distinct clinical situations:</p> <ol style="list-style-type: none"> <li>1. Myocardial perfusion scanning as a technique of identifying perfusion defects which, in turn, reflect coronary artery disease; and</li> <li>2. Assessment of myocardial viability in patients with left ventricular dysfunction as a technique to determine candidacy for a revascularization procedure.</li> </ol> <p><b>Note:</b> Oncology applications and other miscellaneous applications of PET scanning are considered separately in other medical policies.</p> <p><b>Important Note:</b> This policy addresses only the use of radiotracers detected with the use of dedicated PET scanners. Radiotracers such as FDG may be detected using SPECT cameras, a hybrid PET/SPECT procedure that may be referred to as FDG-SPECT, or molecular coincidence detection. FDG-SPECT is considered separately in other medical policies.</p>
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<b>Scope</b>	Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer services representative to determine whether there are any benefit limitations applicable to this service or supply.*
<b>Policy</b>	<p>Cardiac PET scanning may be considered <b>medically necessary</b> to assess myocardial perfusion and thus diagnose coronary artery disease. (See Policy Guidelines regarding the relative effectiveness of PET and SPECT scanning.)</p> <p>Cardiac PET scanning may be considered <b>medically necessary</b> to assess the myocardial viability in patients with severe left ventricular dysfunction as a technique to determine candidacy for a revascularization procedure. (See Policy Guidelines regarding the relative effectiveness of PET and SPECT scanning.)</p>
<b>Policy Guidelines</b>	<p><b>Myocardial Perfusion</b></p> <p>In terms of myocardial perfusion studies, patient selection criteria for PET scans involve an individual assessment of the pretest probability of coronary artery disease, based on both patient symptoms and risk factors. Patients at low risk for coronary artery disease may be adequately evaluated with exercise electrocardiography. Patients at high risk for coronary artery disease may not benefit from a non-invasive assessment of myocardial perfusion, since in this setting, a negative test may represent a false negative result. These patients may be immediately referred to coronary angiography.</p> <p><b>Myocardial Viability</b></p> <p>Patient selection criteria for PET scans for myocardial viability are typically those patients with severe left ventricular dysfunction who are under consideration for a revascularization procedure. A PET scan may determine whether the left ventricular dysfunction is related to viable or non-viable myocardium. Patients with viable myocardium may benefit from revascularization, while those with non-viable myocardium will not. As an example, PET scans are commonly performed in potential heart transplant candidates to rule out the presence of viable myocardium.</p> <p>For both of the above indications, a variety of studies have suggested that PET scans are only marginally more sensitive or specific than SPECT scans. Therefore, the choice between a PET scan (which may not be available locally), and a SPECT scan represents another clinical issue. PET scans may provide the greatest advantage over SPECT scans in obese patients where tissue attenuation of tracer is of greater concern.</p> <p><b>Coding Issues</b></p> <p>A PET scan essentially involves 3 separate activities: 1) Manufacture of the radiopharmaceutical, which may be manufactured on site or manufactured at a regional</p>

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	<p>delivery center with delivery to the institution performing PET; 2) actual performance of the PET scan; and 3) interpretation of the results.</p> <p>The following CPT and HCPC codes are available to code for PET scans:</p> <p><i>CPT codes:</i></p> <p>78459: Myocardial imaging, positron emission tomography (PET) metabolic evaluation. This CPT code describes the use of FDG to evaluate myocardial viability.</p> <p>78491: Myocardial imaging, PET, perfusion: single study at rest or stress</p> <p>78492: Multiple studies at rest and/or stress</p> <p>These 2 CPT codes describe the use of rubidium to evaluate myocardial perfusion.</p> <p>The CPT codes describe the physician component (i.e., interpretation). The technical component may be described by using the “TC” modifier, i.e., 78459-TC. 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, there will likely be an additional transportation charge for radiopharmaceuticals that are not manufactured on site.</p> <p><i>HCPCS Code</i></p> <p>The HCPCS G code for PET are:</p> <p>G0219 PET imaging whole body; full and partial ring PET scanners only, for non-covered indications</p> <p>G0235 PET imaging, any site, not otherwise specified</p>
<p><b>Benefit Application</b></p>	<p><b>Regulatory Status</b></p> <p>The regulatory status of PET scanning and PET scanning facilities has been in flux for many years. The 1997 U.S. Food and Drug Administration (FDA) Modernization Act (FDAMA) attempted to resolve the controversy regarding PET scans first by establishing the FDA authority over the safety and effectiveness of locally manufactured radiotracers and second by developing streamlined regulations for good manufacturing practices (GMP) with which each PET facility must comply.</p> <p>The FDA issued a <i>Federal Register</i> notice on March 10, 2000, summarizing the regulatory history of PET radiotracers and highlighting its decisions on safety and effectiveness for certain uses of certain PET radiotracers. With regard to PET radiotracers used for cardiac indications, the FDA has approved the following uses:</p> <ul style="list-style-type: none"> <li>• <sup>18</sup>F-FDG for evaluation of myocardial hibernation. The FDA concluded that “a 10-mCi dose (for adults) of FDG F 18 injection produced under conditions specified in an approved application can be found to be safe and effective in PET imaging of patients with CAD and left ventricular dysfunction, when used together with</li> </ul>

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myocardial perfusion imaging, for the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function.”

- <sup>13</sup>N-ammonia for evaluation of myocardial blood flow/perfusion. The FDA concluded that “a 10-mCi dose (for adults) of ammonia N 13 injection produced under conditions specified in an approved application can be found to be safe and effective in PET imaging of the myocardium under rest or pharmacological stress conditions to evaluate myocardial perfusion in patients with suspected or existing CAD.”
- In addition, 82-rubidium chloride injection for evaluation of myocardial perfusion (NDA-19-414) was previously approved in 1989 “for assessing regional myocardial perfusion in the diagnosis and localization of myocardial infarction”.

Furthermore, the *Federal Register* notice stipulates that due to safety concerns stemming from various manufacturing practices, “the agency cannot conclude that these PET drugs are generally recognized as safe and effective for the above-noted indications and therefore needs to review information on how each drug product is formulated and produced at each manufacturing site. Because these PET drugs are not generally recognized as safe and effective, they are new drugs for which approved NDA’s or ANDA’s are required for marketing.”

A draft guidance document for Current Good Manufacturing Practice (CGMP) requirements was issued on April 1, 2002; although, as of October 2003, regulatory procedures had not yet been finalized. Manufacturers are not required to submit New Drug Application (NDA) or Abbreviated New Drug Application (ANDA) for a period of 4 years after enactment of the FDA Modernization Act (FDAMA) or “2 years after the date that the agency adopts special approval procedures and CGMP requirements for PET drugs, whichever is longer.” Nevertheless, many PET facilities operate without specific FDA approval. Many plans may have based their coverage policies regarding PET scans on the lack of formal FDA approval rather than on clinical data of safety and effectiveness.

An FDA Web page includes various PET-related documents:  
[www.fda.gov/cder/regulatory/PET](http://www.fda.gov/cder/regulatory/PET). (Accessed August 3, 2006.)

Therefore, as the new regulations are implemented and the FDA reviews the safety and effectiveness of radiotracers, implementation of coverage policies regarding PET scans may need to focus on the following:

- Whether or not the individual PET radiotracer manufacturer facility meets the current good manufacturing practices (CGMP) for PET scanning as established by FDA.
- Whether or not the radiotracer is FDA approved and is being used for a specific indication has been FDA approved.
- Whether or not the clinical indication for individual patients meets medical necessity criteria.

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<p><b>Rationale/ Source</b></p>	<p><b>Introduction</b></p> <p>In 2003, the American College of Cardiology and the American Heart Association (AHA) published updated guidelines for cardiac radionuclide imaging. (1) Cardiac applications of PET scanning were included in these guidelines. The ACC/AHA guidelines categorize specific indications for PET scanning to Class I, Class IIa, Class IIb, or Class III. Class I is defined as conditions for which there is evidence and/or general agreement that a given procedure or treatment is useful and effective. Class IIa is defined as conditions for which there is conflicting evidence or a divergence of opinion but the weight of evidence/opinion is in favor of usefulness/efficacy. Class IIb is similar to Class II except that the usefulness/efficacy is less well established by evidence/opinion. The medically necessary indications for PET myocardial perfusion studies in this policy are consistent with Class I and Class IIa indications in the ACC guidelines.</p> <p><b>Myocardial Viability</b></p> <p>PET has perhaps been most thoroughly researched as a technique to assess myocardial viability to determine candidacy for a coronary revascularization procedure. For example, a patient with a severe stenosis identified by coronary angiography may not benefit from revascularization if the surrounding myocardium is non-viable. A fixed perfusion defect, as imaged on SPECT scanning or stress thallium echocardiography, may suggest non-viable myocardium. However, a PET scan may reveal metabolically active myocardium, suggesting areas of “hibernating” myocardium that would indeed benefit from revascularization. The most common PET technique for this application consists of N-13 ammonia as a perfusion tracer and fluorine-18 fluorodeoxyglucose (FDG) as a metabolic marker of glucose utilization. A pattern FDG uptake in areas of hypoperfusion (referred to as FDG/blood flow mismatch) suggests viable, but hibernating myocardium. The ultimate clinical validation of this diagnostic test is the percentage of patients who experience improvement in left ventricular dysfunction after revascularization of hibernating myocardium, as identified by PET scanning.</p> <p>SPECT scanning may also be used to assess myocardial viability. For example, while initial myocardial uptake of thallium-201 reflects myocardial perfusion, redistribution after prolonged periods can be used as a marker of myocardial viability. Initial protocols required redistribution imaging after 24 to 72 hours. While this technique was associated with a strong positive predictive value, there was a low negative predictive value; i.e., 40% of patients without redistribution nevertheless showed clinical improvement after revascularization. The negative predictive value has improved with the practice of thallium reinjection. Twenty-four to 72 hours after initial imaging, patients receive a reinjection of thallium and undergo redistribution imaging.</p> <p>The ACC/AHA guidelines note that PET imaging “appears to have slightly better overall accuracy for predicting recovery of regional function after revascularization in patients with left ventricular (LV) dysfunction than single photon techniques (i.e., SPECT scans).” However, the ACC guidelines indicate that either PET or SPECT scans are Class I indications for predicting improvement in regional and global LV function and</p>
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natural history after revascularization, and thus do not indicate a clear preference for either PET or SPECT scans in this situation.

Further supporting the equivalency of these 2 testing modalities, Siebelink and colleagues performed a prospective randomized study comparing management decisions and outcomes based on either PET imaging or SPECT imaging in 103 patients with chronic coronary artery disease and left ventricular dysfunction who were being evaluated for myocardial viability. (2) Management decisions included drug therapy or revascularization with either angioplasty or coronary artery bypass grafting. This study is unique in that the diagnostic performance of the 2 studies was tied to the actual patient outcomes. (3) No difference in patient management or cardiac event-free survival was demonstrated between management based on the two imaging techniques. The authors concluded that either technique could be used for management of patients considered for revascularization with suspicion of jeopardized myocardium.

**Myocardial Perfusion**

In a patient with symptoms suggestive of coronary artery disease (CAD), an important clinical decision point is to determine whether a coronary angiogram is necessary for further work-up. A variety of non-invasive imaging tests, including PET (using rubidium-82) and SPECT scans, have been investigated as a means of identifying reversible perfusion defects, which may reflect coronary artery disease, and thus identify patients who may benefit from further work-up with an angiogram. Below is a summary of the ACC guidelines for myocardial reperfusion for both SPECT and PET scans in patients with an intermediate risk of coronary artery disease. (1)

<b>Indication</b>	<b>SPECT Class</b>	<b>PET Class</b>
Identify extent, severity and location of ischemia (SPECT protocols vary according to whether patient can exercise)	I	IIA
Repeat test 3-5 years after revascularization in selected high-risk asymptomatic patients (SPECT protocols vary according to whether patients can exercise)	IIa	
As initial test in patients who are considered to be at high risk (i.e., patients with diabetes or those with a more than 20% 10-year risk of a coronary disease event patients) (SPECT protocols vary according to whether patients can exercise)	IIa	
Myocardial perfusion PET when prior SPECT study has been found to be equivocal for diagnostic or risk stratification purposes	N/A	I

As noted in the above table, the data and consensus opinion (as reflected by a Class I designation) favors limiting a PET scan to those situations in which a prior SPECT scan

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is inconclusive. In the text summary, the guidelines note, "Overall, because of the higher resolution of PET and the routine application of attenuation correction, it is probable that sensitivity and specificity are slightly higher for PET compared with SPECT, but there is not a robust database of head-to-head comparisons." The previous 1995 version of the guidelines stated, "PET is an expensive imaging modality, and whether the greater cost of PET is justified by a possible improvement in diagnostic accuracy requires further rigorous study. Thus, until data from large-scale, definitive studies are published, PET is considered an effective modality for the noninvasive diagnosis of coronary artery disease but should be considered for routine diagnostic purposes only if the costs of PET are equivalent to or less than the costs of SPECT imaging in the same community." (4) This discussion of the relative costs of PET and SPECT has been eliminated in the 2003 version of the guidelines.

### **2006 Update**

A literature review was conducted in May 2006 as part of this update. No clinical trials or studies were found that would alter the policy statements or policy guidelines noted above. Studies continued to show the equivalence of SPECT and PET. As one example, Slart and colleagues concluded that there was overall good agreement between SPECT and PET for the assessment of myocardial viability in patients with severe LV dysfunction. (5). Comparative studies reported on test accuracy and did not address impact on clinical outcomes.

### **Medicare Policy (6,7)**

Beginning October 1, 2002, Medicare will cover FDG PET for the determination of myocardial viability as a primary or initial diagnostic study prior to revascularization, and will continue to cover FDG PET when used as a follow-up to an inconclusive SPECT. However, if a patient received a FDG PET with inconclusive results, a follow-up SPECT is not covered. FDA approved or FDA-cleared full and partial ring PET scanners are covered.

**Limitations:** In the event that a patient receives a SPECT with inconclusive results, a PET scan may be performed and covered by Medicare. However, a SPECT is not covered following a FDG PET with inconclusive results.

**Frequency:** In the absence of national frequency limitations, contractors can, if necessary develop reasonable frequency limitations for myocardial viability.

#### **References:**

1. Klocke FJ, Baird MG, Gateman TM, et al. ACC/AHA/ASNC guidelines for clinical use of cardiac radionuclide imaging: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/ASNC Committee to Revise the 1995 Guidelines for the Clinical Use of Radionuclide Imaging). 2003 American College of Cardiology Web Site. Available at: <http://www.acc.org>. (Accessed March 1, 2005.)

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	<ol style="list-style-type: none"> <li>2. Siebelink HM, Blanksma PK, Crijns HJ et al. No difference in cardiac event-free survival between positron emission tomography-guided and single-photon emission computed tomography-guided management: a prospective, randomized comparison of patients with suspicion of jeopardized myocardium. <i>J Am Coll Cardiol</i> 2001; 37(1):81-8.</li> <li>3. Udelson JE. Testing our tests: surrogate end points versus driving patient management and outcomes. <i>J Am Coll Cardiol</i> 2001; 37(1):89-92.</li> <li>4. Ritchie JL, Bateman TM, Bonow RO et al. Guidelines for clinical use of cardiac radionuclide imaging. <i>J Am Coll Cardiol</i> 1995; 25(2):521-47.</li> <li>5. Slart RH, Bax JJ, de Boer J, et al. Comparison of 99mTc-sestamibi/18FDG DISA SPECT with PET for the detection of viability in patients with coronary artery disease and left ventricular dysfunction. <i>Eur J Nucl Med Mol Imaging</i> 2005;32(8):972-9.</li> <li>6. Medicare Claims Manual, Rev. 113 (04-99), 50-56.</li> <li>7. Medicare Policy: Program Memorandum, Coverage and Related Claims Processing Requirements for Positron Emission Tomography (PET) Scans -for Breast Cancer and Revised Coverage Conditions for Myocardial Viability, Transmittal AB-02-065, May 2, 2002. Accessible at <a href="http://www.cms.hhs.gov/Transmittals/downloads/AB02065.pdf">http://www.cms.hhs.gov/Transmittals/downloads/AB02065.pdf</a>. (Accessed August 3, 2006.)</li> </ol>
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Codes	Number	Description
CPT	78491	Myocardial imaging, positron emission tomography (PET), perfusion; single study at rest or stress
	78492	; multiple studies at rest and/or stress
ICD-9 Procedure	92.05	Cardiovascular and hematopoietic scan and radioisotope function study
ICD-9 Diagnosis	414.00-414.05	Coronary atherosclerosis, code range
	429.9	Heart disease, unspecified
HCPCS	G0219	PET imaging whole body; full and partial ring PET scanners only, for non-covered indications
	G0235	PET imaging any site, not otherwise specified
Type of Service	Radiology	
Place of Service	Outpatient	

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