### Description

Cardiac positron emission tomography (PET) scanning is used in 2 key clinical situations: (1) myocardial perfusion scanning as a technique to identify perfusion defects, which in turn reflect coronary artery disease (CAD); and (2) assessment of myocardial viability in patients with left ventricular (LV) dysfunction as a technique to determine candidacy for a revascularization procedure. Cardiac PET is also being studied in the measurement of myocardial blood flow and blood flow reserve and for evaluation of coronary artery inflammation.

### Related Policies

- Miscellaneous (Noncardiac, Nononcologic) Applications of Positron Emission Tomography
- Oncologic Applications of PET Scanning

### Policy

#### Myocardial Perfusion

Cardiac positron emission tomography (PET) scanning may be considered **medically necessary** to assess myocardial perfusion and thus diagnose coronary artery disease in either of the following conditions:

- In patients with indeterminate single photon emission computed tomography (SPECT) scan
- In patients for whom SPECT could be reasonably expected to be suboptimal in quality on the basis of body habitus. (See Policy Guidelines)

#### Myocardial Viability

Cardiac PET scanning may be considered **medically necessary** to assess 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.)

#### Cardiac Sarcoidosis

Cardiac PET scanning may be considered **medically necessary** for diagnosing cardiac sarcoidosis in patients who are unable to undergo magnetic resonance imaging (MRI) scanning. Examples of patients who are unable to undergo MRI include, but are not limited to, patients with pacemakers, automatic implanted cardioverter-defibrillators (AICDs), or other metal implants.
Policy Guidelines

Myocardial Perfusion Imaging

For myocardial perfusion studies, patient selection criteria for PET scans include individual assessment of the pretest probability of coronary artery disease (CAD), based both on patient symptoms and risk factors. Patients at low risk for CAD may be adequately evaluated with exercise electrocardiography. Patients at high risk for CAD typically will not benefit from noninvasive assessment of myocardial perfusion; a negative test will not alter disease probability sufficiently to avoid invasive angiography. Accordingly, myocardial perfusion imaging is potentially beneficial for patients at intermediate risk of CAD (25%-75% disease prevalence).* This risk can be estimated using the patient’s age, sex, and chest pain quality. For example, Table 1 summarizes a characterization of patient populations at intermediate risk for CAD.(3)

* Intermediate risk ranges used by different authors may differ from the range used here. These pretest probability risk groups are based on a 1995 TEC Assessment(4) and take into account spectrum effect. American College of Cardiology (ACC) guidelines define low risk as less than 10%, intermediate risk as 10% to 90%, and high risk as greater than 90%.

Table 1. Individuals at Intermediate Risk for CAD According to Chest Pain Quality

<table>
<thead>
<tr>
<th>Typical Anginaa</th>
<th>Atypical Anginab</th>
<th>Nonanginal Chest Painb</th>
</tr>
</thead>
<tbody>
<tr>
<td>Men ages 30-39 y</td>
<td>Men ages 30-70 y</td>
<td>Women ages ≥50 y</td>
</tr>
<tr>
<td>Women ages 30-60 y</td>
<td>Women ages ≥50 y</td>
<td>Women ages ≥60 y</td>
</tr>
</tbody>
</table>

a Chest pain with all of the following characteristics: (1) substernal chest discomfort with characteristic quality and duration, (2) provoked by exertion or emotional stress, and (3) relieved by rest or nitroglycerin.
b Chest pain that lacks 1 of the characteristics of typical angina.
c Chest pain that has 1 or none of the typical angina characteristics.

SPECT scanning can be limited by body habitus, particularly by moderate to severe obesity, (body mass index (BMI) > 35 kilograms/square meter (kg/m²)), large breasts, breast implants, previous mastectomy, chest wall deformity, or pleural/pericardial effusion which can cause attenuation of tissue tracer leading to inaccurate images. In patients for whom body habitus is expected to lead to suboptimal SPECT scans, PET scanning is preferred.

Myocardial Viability

Patients selected to undergo PET scans for myocardial viability are typically those with severe left ventricular dysfunction who are being considered for revascularization. A PET scan may determine whether the left ventricular dysfunction is related to viable or nonviable myocardium. Patients with viable myocardium may benefit from revascularization, but those with nonviable myocardium will not. As an example, PET scans are commonly performed in potential heart transplant candidates to rule out the presence of viable myocardium.

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 moderately to severely obese patients for whom tissue attenuation of tracer is of greater concern.
General
PET scans are considered most appropriate in patients with an intermediate risk of coronary artery disease, typically defined as a 25% to 75% probability of having CAD. Clinically, this group of patients typically includes those with chest pain but without a history of myocardial infarction or stroke. Patients at either low or high risk of CAD may not require a myocardial perfusion study at all.

Coding
A PET scan essentially involves 3 separate activities:
- Manufacture of the radiopharmaceutical, which may be manufactured on site or manufactured at a regional delivery center with delivery to the institution performing PET
- Actual performance of the PET scan
- Interpretation of the results.

CPT Code
The following CPT code describes the use of fluorodeoxyglucose (FDG) to evaluate myocardial viability:
- 78459: Myocardial imaging, positron emission tomography (PET) metabolic evaluation

The following 2 CPT codes describe the use of rubidium to evaluate myocardial perfusion:
- 78491: Myocardial imaging, PET, perfusion: single study at rest or stress
- 78492: multiple studies at rest and/or stress

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.

HCPCS
The following are HCPCS codes for FDG, rubidium, and N-13 ammonia:
- 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
- A9526: Nitrogen N-13 ammonia, diagnostic, per study dose, up to 40 millicuries

Benefit Application
Benefit determinations should be based in all cases on the applicable contract language. To the extent there are any conflicts between these guidelines and the contract language, the contract language will control. Please refer to the member’s contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

Some state or federal mandates (e.g., Federal Employee Program (FEP)) prohibit Plans from denying Food and Drug Administration (FDA) - approved technologies as
Medical Policy

investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

**Rationale**

**Background**

PET scans use positron-emitting radionuclide tracers, which simultaneously emit 2 high-energy photons in opposite directions. These photons can be simultaneously detected (referred to as coincidence detection) by a PET scanner, comprising multiple stationary detectors that encircle the thorax. Compared with single-photon emission computed tomography (SPECT) scans, coincidence detection offers greater spatial resolution.

A variety of radionuclide tracers are used for PET scanning, including fluorine-18, rubidium-82, oxygen-15, nitrogen-13, and carbon-11. Most tracers have a short half-life and must be manufactured with an on-site cyclotron. Rubidium-82 is produced by a strontium-82/rubidium-82 generator. The half-life of fluorine-18 is long enough that it can be manufactured commercially at offsite locations and shipped to imaging centers. Radionuclides may be coupled with a variety of physiologically active molecules, such as oxygen, water, or ammonia. Fluorine-18 is often coupled with fluorodeoxyglucose (FDG) to detect glucose metabolism, which in turn reflects metabolic activity, and thus viability, of the target tissue. Tracers that target the mitochondrial complex also are being developed.

**FDA Status**

The U.S. Food and Drug Administration (FDA) issued a Federal Register 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, FDA has approved the following uses:

- **F-18-FDG for evaluation of myocardial hibernation.** 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 myocardial perfusion imaging, for the identification of left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function.”

- **N-13-ammonia for evaluation of myocardial blood flow/perfusion.** 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, rubidium-82-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 [New Drug Application] or ANDA’s [Abbreviated New Drug Application] are required for marketing.”

On December 10, 2009, FDA issued guidance for Current Good Manufacturing Practice (CGMP) for PET drug manufacturers,(1) and in August 2011, FDA issued similar CGMP guidance for small businesses.(2) Compliance with PET CGMP regulations is required 2 years from the date of the earlier guidance, that is, beginning December 10, 2011. As FDA develops new regulations, and reviews radiotracer safety and effectiveness, implementation of Plan policies regarding PET scans may need to focus on the following:

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

Note: This policy only addresses 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. This technique is not discussed in this document.

**Myocardial Perfusion Imaging**

In a patient with symptoms suggesting coronary artery disease (CAD), an important clinical decision point is to determine whether invasive coronary angiography is necessary. A variety of noninvasive imaging tests, including positron emission tomography (PET; using rubidium-82) and single-photon emission computed tomography (SPECT), have been investigated for identifying reversible perfusion defects, which may reflect CAD and thus identify patients appropriately referred for angiography.

Sensitivity and specificity of PET may be slightly better than for SPECT. For example, performance characteristics for PET and SPECT based on the 2007 Canadian Joint Position Statement(5) is shown in Table 2.

**Table 2. Performance Characteristics of PET and SPECT Scanning Based on the 2007 Canadian Joint Position Statement**

<table>
<thead>
<tr>
<th></th>
<th>Positron Emission Tomography</th>
<th>Single-Photon Emission Computed Tomography</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>0.91</td>
<td>0.88</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.89</td>
<td>0.77</td>
</tr>
<tr>
<td>Estimated positive likelihood ratio&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8.27</td>
<td>3.83</td>
</tr>
<tr>
<td>Estimated negative likelihood ratio&lt;sup&gt;b&lt;/sup&gt;</td>
<td>0.10</td>
<td>0.16</td>
</tr>
</tbody>
</table>

<sup>a</sup> Estimated positive likelihood ratio = sensitivity/(1 − specificity).

<sup>b</sup> Estimated negative likelihood ratio = (1 − sensitivity)/specificity.

However, diagnostic utilities of PET and SPECT may be similar (i.e., in terms of modifying disease risk assessment in a manner that affects subsequent decision making in patients with intermediate pretest probability of CAD). For example, as shown in Table 3, a patient with a 50% pretest probability of CAD would have a 9% post-test probability of CAD after
a negative PET scan compared with 13% after a negative SPECT. In either case, further testing likely would not be pursued.

Table 3. Diagnostic Utility (Effect on Pretest CAD Risk Assessment) of PET and SPECT

<table>
<thead>
<tr>
<th>Pretest Probability</th>
<th>Posttest Probability</th>
<th>PET</th>
<th>SPECT</th>
<th>PET</th>
<th>SPECT</th>
</tr>
</thead>
<tbody>
<tr>
<td>30%</td>
<td>Positive Test</td>
<td>78%</td>
<td>62%</td>
<td>4%</td>
<td>6%</td>
</tr>
<tr>
<td></td>
<td>Negative Test</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>50%</td>
<td>Positive Test</td>
<td>89%</td>
<td>79%</td>
<td>9%</td>
<td>13%</td>
</tr>
<tr>
<td></td>
<td>Negative Test</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>70%</td>
<td>Positive Test</td>
<td>95%</td>
<td>90%</td>
<td>19%</td>
<td>27%</td>
</tr>
</tbody>
</table>

PET: positron emission tomography; SPECT: single-photon emission computed tomography.

Posttest probability = posttest odds/(posttest odds + 1).

Posttest odds = pretest odds ´ likelihood ratio.

In 2012, Jaarsma et al reported a meta-analysis comparing the diagnostic performance of noninvasive myocardial perfusion imaging using SPECT, cardiac magnetic resonance imaging (MRI) or PET.(6) The comparison standard was CAD identified with coronary angiography. A total of 166 articles (17,901 patients) met inclusion criteria, with 114 articles on SPECT, 37 on cardiac MRI, and 15 on PET. Sensitivity by patient-level analysis was similar for the 3 tests, with a pooled sensitivity of 88% for SPECT, 89% for MRI, and 84% for PET. Pooled specificity was lower for SPECT (61%), compared with MRI (76%) and PET (81%). Pooled diagnostic odds ratio was 15.31 for SPECT, 26.42 for MRI, and 36.47 for PET. Metaregression indicated that MRI and PET have a significantly higher diagnostic accuracy than SPECT. Although this analysis is limited by potential publication bias for SPECT and significant heterogeneity in the MRI and SPECT studies, most subgroup analyses showed a relative superiority of MRI and PET over SPECT.

A second 2012 meta-analysis by Parker et al(7) compared SPECT and PET stress myocardial perfusion imaging, using coronary angiography as the reference standard. A total of 117 articles met selection criteria. SPECT was assessed in 113 studies (11,212 patients), and PET was assessed in 9 studies (650 patients). Patient-level diagnostic accuracy data were pooled in a bivariate meta-analysis, showing significantly better sensitivity for PET (92.6%) compared with SPECT (88.3%). There was no significant difference in specificity between PET (81.3%) and SPECT (76.0%). The pattern of higher sensitivity for PET over SPECT and similar specificity also was found among higher quality studies.

Another consideration is that there are fewer indeterminate results with PET than SPECT. Bateman et al (2006) retrospectively matched 112 SPECT and 112 PET studies by gender, body mass index (BMI), and presence and extent of CAD, and compared diagnostic accuracy and degree of interpretable certainty (age, 65 years; 52% male; mean BMI, 32 kg/m²; 76% with CAD diagnosed on angiography).(8) Eighteen (16%) of 112 SPECT studies were classified as indeterminate compared with 4 (4%) of 112 PET studies. Liver and bowel uptake were believed to affect 46 (41%) of 112 SPECT studies, compared with 6 (5%) of 112 PET studies. In obese patients (BMI, >30 kg/m²), accuracy of SPECT was 67% versus 85% for PET; accuracy in nonobese patients was 70% for SPECT and 87% for PET. Therefore, for patients with intermediate pretest probability of CAD, one should start with SPECT testing and only proceed to PET in indeterminate cases. In addition, because obese patients are more prone to liver and bowel artifact, PET testing is advantageous over SPECT in severely obese patients.
Merhige et al (2007) reported on noncontemporaneous patients who had similar probabilities of CAD and were evaluated by SPECT or PET. In this single-center study comparing PET with SPECT, patients who received PET scans had lower rates of angiography (13% vs 31% SPECT) and revascularization (6% vs 11% SPECT) with similar rates of death and myocardial infarction at 1-year follow-up. These results are viewed as preliminary, and additional comparative studies showing impact on outcomes are needed.

Section Summary
Evidence on the diagnostic accuracy of PET for myocardial perfusion imaging establishes that PET is at least as good as SPECT in terms of sensitivity and specificity. However, the modest difference in accuracy may not translate to clinically meaningful differences in diagnosis or management, and SPECT remains the first-line test in most instances. For some patients in whom SPECT may be indeterminate due to body habitus or other anatomic factors, PET often can be performed successfully.

Myocardial Viability
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 nonviable. A fixed perfusion defect, as imaged on SPECT scanning or stress thallium echocardiography, may suggest nonviable 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. 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 proportion of patients who experience improvement in left ventricular (LV) dysfunction after revascularization of hibernating myocardium, as identified by PET scanning.

SPECT scanning also may be used to assess myocardial viability. Initial myocardial uptake of thallium-201 reflects myocardial perfusion, and redistribution after prolonged periods can be a marker of myocardial viability. Initial protocols required redistribution imaging after 24 to 72 hours. Although this technique was associated with a strong positive predictive value (PPV), there was a low negative predictive value (NPV) (i.e., 40% of patients without redistribution nevertheless showed clinical improvement after revascularization). NPV 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.

Further supporting the equivalency of these 2 testing modalities, Siebelink et al (2001) performed a prospective randomized study comparing management decisions and outcomes based on either PET imaging or SPECT imaging in 103 patients who had chronic CAD and LV dysfunction and were being evaluated for myocardial viability. Management decisions included drug therapy or revascularization with either angioplasty or coronary artery bypass grafting. This study is unique in that diagnostic performance of PET and SPECT was tied to actual patient outcomes. No difference in patient management or cardiac event-free survival was demonstrated between management based on the 2 imaging techniques. The authors concluded that either technique could be used for management of patients considered for revascularization who have suspicion of jeopardized myocardium.
Studies identified in literature updates continued to show the equivalence of SPECT and PET. Comparative studies reported on test accuracy and did not address impact on clinical outcomes. As 1 example, Slart et al (2005)(11) concluded that there was overall good agreement between SPECT and PET for the assessment of myocardial viability in patients with severe LV dysfunction. Using a thorax-cardiac phantom, Knesaurek and Machac (2006) concluded that PET was better at detecting smaller defects.(12) In this study, a 1-cm insert was not detectable by SPECT, yet it was detectable by PET.

**Section Summary**

PET and SPECT both can be used to assess myocardial viability. Available evidence supports that accuracy of both is roughly similar for this purpose. PET may be more sensitive for small defects, but the clinical significance of identifying small defects is uncertain.

**Myocardial Blood Flow Reserve**

In 2011, Ziadi et al reported a prospective study of the prognostic value of myocardial flow reserve (MFR) with rubidium-82 (Rb-82) PET in 704 consecutive patients.(13) Ninety-six percent of patients (n=677) were followed for a median of 387 days; most (90%) were followed up by telephone. The hypothesis tested was that patients with reduced flow reserve would have higher cardiac event rates and that Rb-82 MFR would be an independent predictor of adverse outcomes. Primary outcome was the prevalence of hard cardiac events (myocardial infarction and cardiac death); secondary outcome was prevalence of major adverse cardiac events (MACE; comprising cardiac death, myocardial infarction, later revascularization, cardiac hospitalization). Patients with a normal Summed Stress Score (SSS) and impaired MFR had a significantly higher incidence of hard events (2% vs 1.3%) and MACE (9% vs 3.8%) compared with patients who had a preserved MFR. Patients with an abnormal SSS and MFR less than 2 had a higher incidence of hard events (11.4% vs 1.1%) and MACE (24% vs 9%) compared with patients who had a preserved MFR. Rb-82 MFR was an independent predictor of cardiac hard events (hazard ratio [HR]=3.3) and MACE (HR=2.4) over SSS. Three patients (0.4%) were classified up and 0 classified down with MFR in the multivariate model (p=0.092).

Murthy et al (2011) examined the prognostic value of Rb-82 PET coronary flow reserve (CFR) in a retrospective series of 2783 patients referred for rest/stress PET myocardial perfusion imaging.(14) CFR was calculated as the ratio of stress to rest myocardial blood flow using semiquantitative PET interpretation. Primary outcome was cardiac death over a median follow-up of 1.4 years. Prognostic modeling was done with a Cox proportional hazards model. Adding CFR to a multivariate model significantly improved model fit and improved the c index, a measure of discrimination performance, from 0.82 to 0.84 (p=0.02). CFR was a significant independent predictor of cardiac mortality and resulted in improved risk reclassification. In 2012, these authors reported that the added value of PET CFR was observed in both diabetic and nondiabetic patients.(15)

Other publications describe the use of PET imaging to quantify both myocardial blood flow and MFR.(16,17) However, as noted in an accompanying editorial(18) and by subsequent reviewers(19), larger prospective clinical trials are needed to understand the clinical utility.

**Cardiac Sarcoidosis**

Based on clinical input received in 2011, an additional indication for the workup of cardiac sarcoidosis was added to the policy. Published evidence on utility of PET scanning for cardiac sarcoidosis is limited due to the relatively small number of patients with this condition. A 2009 review by Shrama et al concluded that imaging studies had
incremental value when combined with clinical evaluation and/or myocardial biopsy in the diagnosis of cardiac sarcoidosis. The authors reported that cardiac MRI was the more established imaging modality in diagnosing sarcoidosis, with an estimated sensitivity of 100% and specificity of 80%. A 2012 meta-analysis by Yousef et al identified 7 studies with 164 patients. Studies were selected if they used FDG PET for diagnosis of cardiac sarcoidosis and used criteria of the Japanese Ministry of Health, Labor and Welfare as the reference standard. Pooled sensitivity of PET by random effects meta-analysis was 89% and pooled specificity was 78%. Area under the summary receiver operating characteristic curve was 93%, suggesting a good level of diagnostic discrimination.

Summary

Evidence from the medical literature supports the use of positron emission tomography (PET) scanning to assess myocardial viability in patients with severe left ventricular dysfunction who are being considered for revascularization. Results of primary studies and recommendations from specialty societies conclude that PET scanning is at least as good as, and likely superior, to single photon emission computed tomography (SPECT) scanning for this purpose. For assessing myocardial perfusion in patients with suspected coronary artery disease, PET scanning is less likely than SPECT scanning to provide indeterminate results. Therefore, PET scanning also is useful in patients with an indeterminate SPECT scan. It also is useful in patients whose body habitus is likely to result in indeterminate SPECT scans, for example patients with moderate to severe obesity. For patients who are undergoing a workup for cardiac sarcoidosis, magnetic resonance imaging (MRI) is the preferred initial test. However, for patients who are unable to undergo MRI, such as patients with a metal implant, PET scanning is the preferred test.

Ongoing Clinical Trials

A search of online site, ClinicalTrials.gov, revealed an ongoing randomized controlled trial of cardiac imaging in ischemic heart failure (NCT01288560). This study has an estimated enrollment of 1261 and is expected to be completed in March 2016. It includes patients with CAD and heart failure with a left ventricular ejection fraction of 45% or less. Patients are randomized to management algorithms guided either by SPECT or PET/MRI.

The ongoing, single-blind (assessor) CENTURY trial is a randomized lifestyle modification study for management of stable coronary artery disease (NCT00756379). A PET perfusion imaging-guided intensive lifestyle modification program will be compared with standard medical management. Although all patients will undergo PET perfusion imaging at baseline and at intervals throughout the trial, PET results for patients in the standard treatment arm will be blinded until the end of the study.

Practice Guidelines and Position Statements

American College of Cardiology/American Heart Association

In 2003, ACC and AHA published updated guidelines for cardiac radionuclide imaging, including cardiac applications of PET.(22) Table 4 summarizes the guidelines for PET and SPECT imaging in patients with an intermediate risk of coronary artery disease (CAD). 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.
Table 4. American College of Cardiology/American Heart Association 2003 Guidelines for PET and SPECT Imaging in Patients with Intermediate Coronary Artery Disease Risk(22)

<table>
<thead>
<tr>
<th>Indication</th>
<th>SPECT Class</th>
<th>PET Class</th>
</tr>
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<tbody>
<tr>
<td>Identify extent, severity, and location of ischemia (SPECT protocols vary</td>
<td>I</td>
<td>Ila</td>
</tr>
<tr>
<td>according to whether patient can exercise)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Repeat test after 3-5 y after revascularization in selected high-risk</td>
<td>Ila</td>
<td>–</td>
</tr>
<tr>
<td>asymptomatic patients (SPECT protocols vary according to whether patients</td>
<td></td>
<td></td>
</tr>
<tr>
<td>can exercise)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>As initial test in patients who are considered to be at high risk (i.e.,</td>
<td>Ila</td>
<td>–</td>
</tr>
<tr>
<td>patients with diabetes or those with a &gt;20% 10-y risk of a coronary disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>event) (SPECT protocols vary according to whether patients can exercise)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Myocardial perfusion PET when prior SPECT study has been found to be</td>
<td>NA</td>
<td>I</td>
</tr>
<tr>
<td>equivocal for diagnostic or risk stratification purposes</td>
<td></td>
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PET: positron emission tomography; SPECT: single-photon emission computed tomography.

These guidelines concluded that PET imaging “appears to have slightly better overall accuracy for predicting recovery of regional function after revascularization in patients with left ventricular dysfunction than single photon techniques (i.e., SPECT scans).”(22) However, the guidelines indicate that either PET or SPECT scans are class I indications for predicting improvement in regional and global LV function and natural history after revascularization and thus do not indicate a clear preference for either PET or SPECT scans in this situation.

**Canadian Cardiovascular Society et al**

In 2005, Canadian Cardiovascular Society, Canadian Association of Radiologists, Canadian Association of Nuclear Medicine, Canadian Nuclear Cardiology Society, and Canadian Society of Cardiac Magnetic Resonance recommended PET scanning for patients with intermediate pretest probability of CAD who have nondiagnostic noninvasive imaging tests, or where such a test does not agree with clinical diagnosis or may be prone to artifact that could lead to an equivocal other test (e.g., obesity) (Class I recommendation, level B evidence).(5)

**American College of Radiology**

The 2011 American College of Radiology (ACR) Appropriateness Criteria consider both SPECT and PET to be appropriate for the evaluation of patients with a high probability of CAD.(23) ACR states that PET perfusion imaging has advantages over SPECT, including higher spatial and temporal resolution. Routine performance of both PET and SPECT are unnecessary.

**European Society of Cardiology**

European Society of Cardiology published evidence-based consensus guidelines for the diagnosis and treatment of acute and chronic heart failure in 2012.(24) Guideline authors concluded that myocardial perfusion/ischemia imaging should be considered in patients thought to have CAD, who are considered suitable for coronary revascularization, to determine whether there is reversible myocardial ischemia and viable myocardium. Recommended imaging modalities are echocardiography, cardiac MRI, SPECT, and PET. (Class 2a recommendation [weight of evidence/opinion is in favor of usefulness/efficacy]; level C evidence [based on consensus expert opinion and/or small or retrospective studies or registries].)
Japanese Society of Nuclear Cardiology

In 2014, the Japanese Society of Nuclear Cardiology published recommendations for PET imaging for cardiac sarcoidosis.(25) In Japan, F-18-FDG PET is approved only for detecting sites of inflammation in cardiac sarcoidosis. In patients with cardiac sarcoidosis diagnosed by established guidelines (e.g., 2006 update of JMHW guidelines), FDG PET may be used to assess lesion distribution. However, use of FDG PET to diagnose patients with suspected cardiac sarcoidosis is not covered by the health ministry's insurance reimbursement.

U.S. Preventive Services Task Force

No U.S. Preventive Services Task Force recommendations for the use of PET in cardiac imaging were identified.

Medicare National Coverage

Beginning October 1, 2002, Medicare will cover FDG PET for the determination of myocardial viability as a primary or initial diagnostic study before revascularization and will continue to cover FDG PET when used as follow-up to an inconclusive SPECT.(26) However, if a patient received 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, SPECT is not covered after 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


24. Authors/Task Force Members: McMurray JJ, Adamopoulos S, Anker SD et al. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. Eur Heart J 2012; 33(14):1787-847.


**Documentation Required for Clinical Review**

- History and physical and/or consultation notes including:
  - Indication for PET scan
  - Previous treatment and response
- Previous Imaging reports (e.g., CT, MRI, SPECT)
- Reason patient is unable to undergo MRI (if applicable)

**Post Service**

- PET report

**Coding**

This Policy relates only to the services or supplies described herein. Benefits may vary according to benefit design; therefore, contract language should be reviewed before applying the terms of the Policy. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement.

**MN/NMN**

The following services may be considered medically necessary when policy criteria are met. Services are considered not medically necessary when policy criteria are not met.
## Medical Policy

<table>
<thead>
<tr>
<th>Type</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CPT®</strong></td>
<td>78459</td>
<td>Myocardial imaging, positron emission tomography (PET), metabolic evaluation</td>
</tr>
<tr>
<td></td>
<td>78491</td>
<td>Myocardial imaging, positron emission tomography (PET), perfusion; single study at rest or stress</td>
</tr>
<tr>
<td></td>
<td>78492</td>
<td>Myocardial imaging, positron emission tomography (PET), perfusion; multiple studies at rest and/or stress</td>
</tr>
<tr>
<td><strong>HCPC</strong></td>
<td>A9526</td>
<td>Nitrogen n-13 ammonia, diagnostic, per study dose, up to 40 millicuries</td>
</tr>
<tr>
<td></td>
<td>A9552</td>
<td>Fluorodeoxyglucose F-18 FDG, diagnostic, per study dose, up to 45 millicuries</td>
</tr>
<tr>
<td></td>
<td>A9555</td>
<td>Rubidium rb-82, diagnostic, per study dose, up to 60 millicuries</td>
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</table>

<table>
<thead>
<tr>
<th>ICD Procedure</th>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ICD-10 Procedure</strong></td>
<td>92.05</td>
<td>Cardiovascular and hematopoietic scan and radioisotope function study</td>
</tr>
<tr>
<td><strong>ICD-9 Procedure</strong></td>
<td>C23GKZZ</td>
<td>Positron Emission Tomographic (PET) Imaging of Myocardium using Fluorine 18 (F-18)</td>
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<td>C23GMZZ</td>
<td>Positron Emission Tomographic (PET) Imaging of Myocardium using Oxygen 15 (O-15)</td>
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<td></td>
<td>C23GQZZ</td>
<td>Positron Emission Tomographic (PET) Imaging of Myocardium using Rubidium 82 (Rb-82)</td>
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<td>C23GRZZ</td>
<td>Positron Emission Tomographic (PET) Imaging of Myocardium using Nitrogen 13 (N-13)</td>
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<tr>
<td></td>
<td>C23GYZZ</td>
<td>Positron Emission Tomographic (PET) Imaging of Myocardium using Other Radionuclide</td>
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<tr>
<td></td>
<td>C23YYZZ</td>
<td>Positron Emission Tomographic (PET) Imaging of Heart using Other Radionuclide</td>
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</table>

<table>
<thead>
<tr>
<th>ICD Diagnosis</th>
<th>Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td><strong>ICD-9 Diagnosis</strong></td>
<td>All Diagnoses</td>
<td>For dates of service on or after 10/01/2015</td>
</tr>
<tr>
<td><strong>ICD-10 Diagnosis</strong></td>
<td>All Diagnoses</td>
<td>For dates of service on or after 10/01/2015</td>
</tr>
</tbody>
</table>

### Policy History

This section provides a chronological history of the activities, updates and changes that have occurred with this Medical Policy.

<table>
<thead>
<tr>
<th>Effective Date</th>
<th>Action</th>
<th>Reason</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/15/2014</td>
<td>Policy title change from Positron Emission Tomography (PET)</td>
<td>Medical Policy Committee</td>
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<tr>
<td></td>
<td>Policy revision with position change</td>
<td></td>
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</tbody>
</table>
Definitions of Decision Determinations

**Medically Necessary:** A treatment, procedure or drug is medically necessary only when it has been established as safe and effective for the particular symptoms or diagnosis, is not investigational or experimental, is not being provided primarily for the convenience of the patient or the provider, and is provided at the most appropriate level to treat the condition.

**Investigational/Experimental:** A treatment, procedure or drug is investigational when it has not been recognized as safe and effective for use in treating the particular condition in accordance with generally accepted professional medical standards. This includes services where approval by the federal or state governmental is required prior to use, but has not yet been granted.

**Split Evaluation:** Blue Shield of California / Blue Shield of California Life & Health Insurance Company (Blue Shield) policy review can result in a Split Evaluation, where a treatment, procedure or drug will be considered to be investigational for certain indications or conditions, but will be deemed safe and effective for other indications or conditions, and therefore potentially medically necessary in those instances.

Prior Authorization Requirements

This service (or procedure) is considered medically necessary in certain instances and investigational in others (refer to policy for details).

For instances when the indication is medically necessary, clinical evidence is required to determine medical necessity.

For instances when the indication is investigational, you may submit additional information to the Prior Authorization Department.

Within five days before the actual date of service, the Provider MUST confirm with Blue Shield that the member's health plan coverage is still in effect. Blue Shield reserves the right to revoke an authorization prior to services being rendered based on cancellation of the member's eligibility. Final determination of benefits will be made after review of the claim for limitations or exclusions.

Questions regarding the applicability of this policy should also be directed to the Prior Authorization Department. Please call 1-800-541-6652 or visit the Provider Portal www.blueshieldca.com/provider.

The materials provided to you are guidelines used by this plan to authorize, modify, or deny care for persons with similar illness or conditions. Specific care and treatment may vary depending on individual need and the benefits covered under your contract. These Policies are subject to change as new information becomes available.