6.01.20	Cardiac Applications of Positron Emission Tomography Scanning		
Original Policy Date:	December 15, 2014	**Effective Date:**	January 1, 2018
Section:	6.0 Radiology	**Page:**	Page 1 of 24

Policy Statement

Myocardial Perfusion
Cardiac positron emission tomography (PET) scanning may be considered **medically necessary** to assess myocardial perfusion and thus diagnose coronary artery disease (CAD) in **either** of the following conditions:
- Patients with indeterminate single-photon emission computed tomography (SPECT) scan
- Patients for whom SPECT could be reasonably expected to be suboptimal in quality on the basis of body habitus. (See Policy Guidelines section)

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 the Policy Guidelines section 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 magnetic resonance imaging include, but are not limited to, patients with pacemakers, automatic implanted cardioverter defibrillators, or other metal implants.

Cardiac PET scanning is **investigational** for quantification of myocardial blood flow in patients diagnosed with coronary artery disease.

Policy Guidelines

Positron Emission Tomography
Positron emission tomography (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.

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).[1]* Risk can be estimated using the patient's age, sex, and chest pain quality. Table 1 summarizes patient populations at intermediate risk for CAD. [2]

*Intermediate-risk ranges used in different studies may differ from the range used here. These pretest probability risk groups are based on a 1995 TEC Assessment and take into account spectrum effect. American College of Cardiology guidelines have defined 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 Coronary Artery Disease According to Chest Pain Quality

Populations	Typical Angina[a]	Atypical Angina[b]	Nonanginal Chest Pain[c]
Men	ages 30-39 y	ages 30-70 y	ages ≥50 y
Women	ages 30-60 y	ages ≥50 y	ages ≥60 y

CAD: coronary artery disease.
[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 one of the characteristics of typical angina.
[c] Chest pain that has one or none of the typical angina characteristics.

Body habitus can limit SPECT; particularly moderate-to-severe obesity, (body mass index [BMI] greater than 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 scanning 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 scanning is commonly performed in potential heart transplant candidates to rule out the presence of viable myocardium.

Comparison Between Positron Emission Tomography and Single-Photon Emission Computed Tomography
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 presents 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. Table 2 summarizes differences between cardiac SPECT and PET techniques.[3]

Table 2. Advantages and Disadvantages of Cardiac Positron Emission Tomography and Single-Photon Emission Computed Tomography[3]

Imaging Technique	Advantages	Disadvantages
PET	• Superior diagnostic capability, particularly for obese patients and patients with multivessel disease • Quantifiable blood flow evaluation • Integration of functional and anatomic information • Better spatial and contrast resolution • Lower frequency of artifacts	• Higher equipment cost • Cyclotron or rubidium generators required • Radiotracers with short physical half-life do not permit exercise stress testing
SPECT	• Wide availability • Well-established through published studies and familiar worldwide • Lower equipment cost • Less expensive radiotracers • Combined with dynamic exercise stress testing	• Longer acquisition duration • Lower resolution images due to artifacts and attenuation • Higher radiation burden

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

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 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.

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 positron emission tomography (PET) scan 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, positron emission tomography (PET), perfusion: single study at rest or stress
- **78492**: Myocardial imaging, positron emission tomography (PET), perfusion; multiple studies at rest and/or stress

Effective January 1, 2018, the following CPT code is considered an add-on code and may be reported with code 78491 or 78492:
- **0482T**: Absolute quantitation of myocardial blood flow, positron emission tomography (PET), rest and stress (List separately in addition to code for primary procedure)

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. Also, 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

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Description

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multiple stationary detectors that encircle the thorax. Compared with single-photon emission computed tomography (SPECT) scans, coincidence detection offers greater spatial resolution. PET has been investigated as an option to diagnose and evaluate patients with cardiac conditions such as coronary artery disease, left ventricular dysfunction, and cardiac sarcoidosis.

Related Policies

- Interim Positron Emission Tomography Scanning in Oncology to Detect Early Response During Treatment
- Miscellaneous (Noncardiac, Nononcologic) Applications of Fluorodeoxyglucose F 18 Positron Emission Tomography
- Oncologic Applications of Positron Emission Tomography Scanning

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)] prohibits plans from denying Food and Drug Administration (FDA)-approved technologies as investigational. In these instances, plans may have to consider the coverage eligibility of FDA-approved technologies on the basis of medical necessity alone.

Regulatory Status

A number of PET platforms have been cleared by the U.S. Food and Drug Administration (FDA) through the 510(k) process since the Penn-PET scanner was approved in 1989. These systems are intended to aid in detecting, localizing, diagnosing, staging, and restaging of lesions, tumors, disease, and organ function for the evaluation of diseases and disorders such as, but not limited to, cardiovascular disease, neurologic disorders, and cancer. The images produced by the system can aid in radiotherapy treatment planning and interventional radiology procedures. PET radiopharmaceuticals have been evaluated and approved by the FDA for use as diagnostic imaging agents. These radiopharmaceuticals are approved for specific conditions.

In December 2009, the FDA issued guidance for Current Good Manufacturing Practice for PET drug manufacturers,[4] and in August 2011, the FDA issued similar Current Good Manufacturing Practice guidance for small businesses.[5] An additional final guidance document issued in December 2012 required all PET drug manufacturers and compounders to operate under an approved new drug application (NDA) or abbreviated NDA, or investigational new drug application, by December 2015.[6]

To avoid interruption of the use of PET radiotracers already in use in clinical practice, before the issuance of specific guidance documents, the FDA made determinations of safety and effectiveness for certain uses of PET radiotracers.

The following radiopharmaceuticals used with PET for cardiac-related indications were reviewed in this manner and subsequently had approved NDAs as summarized in Table 3.

Table 3. Radiopharmaceuticals Approved for Use with Positron Emission Tomography for Cardiac Indications

Date Approved	Radiopharmaceutical	Manufacturer	NDA	Cardiac-Related Indication with Positron Emission Tomography
2000	Fluorine 18 fluorodeoxyglucose (F-18-FDG)	Various	20306	CAD and left ventricular dysfunction, when used with myocardial perfusion imaging, to identify left ventricular myocardium with residual glucose metabolism and reversible loss of systolic function
2000	Ammonia N 13	Zevacor Pharma	22119	Imaging of the myocardium under rest or pharmacologic stress conditions to evaluate myocardial perfusion in patients with suspected or existing CAD
1989	Rubidium 82 chloride	Bracco Diagnostics	19414	Assessing regional myocardial perfusion in the diagnosis and localization of myocardial infarction

CAD: coronary artery disease; NDA: new drug application; PET: positron emission tomography.

Rationale

Background
Positron Emission Tomography
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Literature Review

Assessment of a diagnostic technology typically focuses on 3 categories of evidence: (1) technical reliability (test-retest reliability or interrater reliability); (2) clinical validity (sensitivity, specificity, and positive and negative predictive value) in relevant populations of patients; and (3) clinical utility (ie, demonstration that the diagnostic information can be used to improve patient outcomes). The following is a summary of the key literature to date.

Positron Emission Tomography
Clinical Context and Test Purpose
The purposes of positron emission tomography (PET) scanning in patients with suspected coronary artery disease (CAD), left ventricular (LV) dysfunction who are potential candidates for revascularization, CAD who require myocardial blood flow (MBF) quantification, and cardiac sarcoidosis are to confirm a diagnosis or to inform a clinician in disease management decisions.

The question addressed in this evidence review is: Does the use of PET improve the net health outcome in individuals with suspected CAD, LV dysfunction considering revascularization, CAD in need of MBF quantification, and cardiac sarcoidosis?

The following Patients, Interventions, Comparators, Outcomes, Timing, and Setting (PICOTS) were used to select literature to inform this review.

Patients
The population of interest includes patients with suspected CAD who have indeterminate single-photon emission computed tomography (SPECT) scans, severe LV dysfunction who are potential candidates for revascularization, CAD in need of quantifying MBF, and cardiac sarcoidosis who cannot undergo magnetic resonance imaging (MRI).

Interventions
The intervention of interest is PET scanning.

Comparators
The comparators of interest for each indication include:
- For suspected CAD, coronary angiography or other noninvasive tests for CAD (e.g., stress echocardiography, exercise electrocardiography)
- For severe LV dysfunction, cardiac MRI or cardiac SPECT scanning
- For quantifying MBF in patients with CAD, coronary angiography with fractional flow reserve (FFR) or clinical risk models
- For cardiac sarcoidosis, clinical evaluation or myocardial biopsy

Outcomes
For patients with suspected CAD, the outcome of interest is confirmed diagnosis. With a confirmed diagnosis, appropriate treatment options can be pursued.

For patients with severe LV dysfunction who are potential candidates for revascularization, the outcome of interest is a viability assessment. If there is sufficient viable myocardium detected, the patient would be a candidate for revascularization.

For patients with CAD who require MBF quantification, the outcome of interest is accurate quantification to inform clinical management of the disease.

For patients with suspected or diagnosed cardiac sarcoidosis, the outcome of interest is a diagnosis confirmation or an assessment of disease activity to inform clinical management of the disease.

Timing
For suspected CAD, MBF quantification, and suspected cardiac sarcoidosis, the timing of the test would be during the disease confirmation process. For severe LV dysfunction, the timing would be prior to surgical (revascularization) and clinical decision making.

Setting
The setting is an imaging center equipped with a PET scanner.

Suspected Coronary Artery Disease
Technical Reliability

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

The sensitivity and specificity of PET may be slightly better than for SPECT. Performance characteristics for PET and SPECT based on a 2007 Canadian joint position statement[7] are shown in Table 4.

Table 4. Performance Characteristics of Positron Emission Tomography and Single-Photon Emission Computed Tomography Based on the 2007 Position Statement[7]

Outcome Measures	PET	SPECT
Sensitivity	91%	88%
Specificity	89%	77%
Estimated positive likelihood ratio[a]	8.27	3.83
Estimated negative likelihood ratio[b]	0.10	0.16

PET: positron emission tomography; SPECT: single-photon emission computed tomography.
[a] Estimated positive likelihood ratio = sensitivity/(1 − specificity).
[b] Estimated negative likelihood ratio = (1 − sensitivity)/specificity.

However, diagnostic utilities of PET and SPECT may be similar 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 5, a patient with a 50% pretest probability of CAD would have a 9% posttest probability of CAD after a negative PET scan compared with 13% probability after a negative SPECT. In either case, further testing may not be pursued.

Table 5. Diagnostic Utility (Effect on Pretest Coronary Artery Disease Risk Assessment) of Positron Emission Tomography and Single-Photon Emission Computed Tomography

Pretest Probability	Posttest Probability, %			
	Positive Test		Negative Test	
	PET	SPECT	PET	SPECT
30%	78	62	4	6
50%	89	79	9	13
70%	95	90	19	27

CAD: coronary artery disease; PET: positron emission tomography; SPECT: single-photon emission computed tomography.

Clinical Validity
Systematic Reviews

In 2016, Dai et al conducted a meta-analysis comparing the abilities of the following cardiac imaging modalities in diagnosing CAD: SPECT, PET, dobutamine stress echocardiography, cardiac MRI, and computed tomography (CT) perfusion imaging.[8] The reference standard was FFR derived from CT. The literature search, conducted through June 2015, identified 74 studies for inclusion, 5 of which used PET. Study quality was assessed using Standards for Reporting Diagnostic Accuracy and Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tools. Pooled sensitivity and specificity for PET were 90% (95% confidence interval [CI], 80% to 95%) and 84% (95% CI, 81% to 90%). These rates were similar to FFR, the reference standard (sensitivity, 90% [95% CI, 85% to 93%]; specificity, 75% [95% CI, 62% to 85%]).

In 2012, Jaarsma et al reported on a meta-analysis comparing the diagnostic performance of noninvasive myocardial perfusion imaging using SPECT, cardiac MRI, or PET.[9] The comparison standard was CAD identified with coronary angiography. A total of 166 articles (N=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%) or PET (81%). The pooled diagnostic odds ratio was 15.31 for SPECT, 26.42 for MRI, and 36.47 for PET. Meta-regression indicated that MRI and PET have a significantly higher diagnostic accuracy than SPECT. Although this analysis was limited by potential publication bias for SPECT and significant heterogeneity in the MRI and SPECT studies, most subgroup analyses have shown a relative superiority of MRI and PET over SPECT.

A second 2012 meta-analysis, by Parker et al, compared SPECT with PET stress myocardial perfusion imaging, using coronary angiography as the reference standard.[10] A total of 117 articles met selection criteria. SPECT was assessed in 113 studies (n=11,212 patients), and PET was assessed in 9 studies (n=650 patients). Patient-level diagnostic accuracy data were pooled in a bivariate meta-analysis, showing significantly better sensitivity for PET (92.6%) than for SPECT (88.3%). The difference in specificity between PET (81.3%) and SPECT (76.0%) was not significant. The pattern of higher sensitivity for PET over SPECT and similar specificity remained when analyses were limited to only high-quality studies.

Takx et al (2015) reported a meta-analysis of studies that compared noninvasive myocardial perfusion imaging modalities (MRI, CT, PET, SPECT, echocardiography) with coronary angiography plus FFR.[11] Literature was searched to May 2014, and 37 studies met inclusion criteria (total N=4698 vessels). Three PET studies of moderate-to-high quality were included (870 vessels); pretest probability of CAD was intermediate to intermediate-high in these studies. Negative likelihood ratio (NLR) was chosen as the primary outcome of interest because ruling out hemodynamically significant CAD is a primary purpose of noninvasive imaging. At the vessel level, pooled NLRs for PET, MRI, and CT were similar and were lower (better) than the pooled NLR for SPECT (PET pooled NLR=0.15 [95% CI, 0.05 to 0.44]; SPECT pooled NLR=0.47 [95% CI, 0.37 to 0.59]). Similarly, at the patient level, pooled NLRs for PET, MRI, and CT were better than the pooled NLRs for SPECT and echocardiography (PET pooled NLR=0.14 [95% CI, 0.02 to 0.87]; SPECT pooled NLR=0.39 [95% CI, 0.27 to 0.55]). The area under the receiver operating characteristic (AUROC) analyses were similar at both the vessel level (PET, 0.95 vs SPECT, 0.83) and the patient level (PET, 0.93 vs SPECT, 0.82).

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 sex, body mass index, and presence and extent of CAD, and compared diagnostic accuracy and degree of interpretative certainty (age, 65 years; 52% male; mean body mass index, 32 kg/m²; 76% with CAD diagnosed on angiography).[12] 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 (body mass index, >30 kg/m²), the accuracy of SPECT was 67% and 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. Also, because obese patients are more prone to liver and bowel artifact, PET testing is advantageous over SPECT in these patients.

Clinical Utility
Systematic Reviews
In 2017, Chen et al published a meta-analysis assessing the prognostic value of PET myocardial perfusion imaging in patients with known or suspected CAD.[13] For inclusion, studies had to have at least one of the following outcomes: mortality, cardiac infarction, or major adverse cardiac event (MACE). The literature search, conducted through June 2016, identified 11 studies for inclusion. Quality assessment was based on: (1) cohort follow-up of 90% or more; (2) blinded outcome assessors; and (3) corroboration of outcomes with hospital records or death certificates. Nine of the studies were of good quality, and two were fair. All 11 studies included cardiac death as the primary or secondary outcome, with a pooled negative predictive value

(NPV) of 99% (95% CI, 98% to 99%). Seven studies included all-cause death as an outcome, with a pooled NPV of 95% (95% CI, 93% to 96%). Four studies included MACE as an outcome, with a pooled NPV of 90% (95% CI, 78% to 96%).

In 2017, Smulders et al published a meta-analysis comparing the prognostic value of the following negative noninvasive cardiac tests: coronary computed tomography angiography, cardiovascular MRI, exercise electrocardiographic testing, PET, stress echocardiography, and SPECT.[14] Outcomes of interest were annual event rates of myocardial infarction and cardiac death. The literature search, conducted through April 2015, identified 165 studies for inclusion, four of which involved PET. Study quality was assessed using the Newcastle-Ottawa Scale for observational studies. Pooled annual event rates for cardiac death and myocardial infarction for PET were low (0.41; 95% CI, 0.15 to 0.80), indicating that a patient with a negative PET test has a good prognosis.

Section Summary: Suspected Coronary Artery Disease
Evidence on the diagnostic accuracy of PET for CAD consists of several systematic reviews and meta-analyses. Meta-analyses comparing PET with reference standards such as coronary angiography and FFR have shown that PET is comparable in diagnostic accuracy. Meta-analyses that have evaluated the clinical utility of PET have looked at outcomes such as mortality and adverse cardiac events. These meta-analyses have shown that PET is a useful prognostic tool. For some patients in whom SPECT may be indeterminate due to body habitus or other anatomic factors, PET can be performed successfully.

Severe Left Ventricular Dysfunction Considering Revascularization
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 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, there was a low NPV; i.e., 40% of patients without redistribution nevertheless showed clinical improvement after revascularization. NPVs have 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.

Clinical Validity
Studies identified in literature have shown the equivalence of SPECT and PET in their ability to assess myocardium viability. Comparative studies have reported on test accuracy and have not addressed the impact on clinical outcomes.

Using a thorax-cardiac phantom with different sized inserts that simulated infarcts, Knesaurek and Machac (2006) tested SPECT and PET images.[15] The investigators concluded that PET was better at detecting smaller defects than SPECT. In this study, a 1-cm insert, not detected by SPECT, was detected by PET.

Slart et al (2005) compared dual-isotope simultaneous acquisition SPECT and PET in the detection of myocardial viability in 58 patients with CAD and dysfunctional LV myocardium.[16] Tracer uptake for PET and SPECT was compared by linear regression and correlation analysis, which showed that there was overall good agreement between SPECT and PET for the assessment of myocardial viability in patients with severe LV dysfunction.

Clinical Utility
Randomized Controlled Trials
A large randomized controlled trial, Positron Emission Tomography and Recovery Following Revascularization (PARR-2), evaluated the impact of FDG-PET viability imaging on patients with severe LV dysfunction. Patients from 9 sites were randomized to FDG-PET-assisted physician management (n=218) or standard care management by a physician without PET imaging available (n=212). Management decision options were: revascularization, revascularization workup, or neither. The primary outcome was a composite of cardiac death, myocardial infarction, or recurrent hospital stay for a cardiac cause. Beanlands et al (2007) reported on results after 1 year of follow-up.[17] The intention-to-treat hazard ratio (HR) of a composite event occurring at 1 year was not significant (0.78; 95% CI, 0.58 to 1.1; p=0.15) for PET-assisted management of care compared with standard care. However, among patients in the PET-assisted management of care group who had high or medium myocardium viability and who therefore were recommended to receive revascularization or a revascularization workup, 26% did not ultimately receive the recommended care. Reasons given included symptoms stabilizing, renal failure, multiple comorbidities, and patient refusal. When subgroup analysis included only those patients who received the treatment as recommended based on PET images, the HR for a composite event was significant (0.62; 95% CI, 0.42 to 0.93).

In 2016, Mc Ardle et al published long-term follow-up results for PARR-2.[18] Six of the 9 original sites participated in the long-term follow-up study (197 patients in the PET-assisted arm, 195 patients in the standard care arm). Long-term results were similar to the 1-year results. The HR for time to composite event for the whole study population did not differ significantly between the PET-assisted group and the standard care group (0.82; 95% CI, 0.62 to 1.1); however, when analysis was conducted using only the subgroup of patients who adhered to the PET imaging-based recommendations, the HR was statistically significant (0.73; 95% CI, 0.54 to 0.99).

Siebelink et al (2001) performed a prospective randomized study comparing management decisions with outcomes based on PET imaging (n=49) or SPECT imaging (n=54) in patients who had chronic CAD and LV dysfunction and were being evaluated for myocardial viability.[19] Management decisions based on readings of the PET or SPECT images included either drug therapy for patients without viable myocardium or revascularization with either angioplasty or coronary artery bypass grafting (CABG) for patients with viable myocardium. 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 to manage patients considered for revascularization.

Nonrandomized Study
In 2016, Srivatsava et al published a study of 120 patients with LV dysfunction who underwent both SPECT-CT and FDG-PET/CT to determine myocardial viability.[20] If both tests showed defects, the tissue was considered nonviable. If test results were mismatched, the tissue was considered hibernating but viable. If more than 7% of the myocardium was considered viable, patients underwent revascularization by either stenting or CABG (78 patients). Patients assessed as having less than 7% viable myocardium were medically managed (42 patients). The primary outcome was global left ventricular ejection fraction (LVEF). Change in LVEF after 3 months was significantly larger in the surgically managed group (3.5; 95% CI, 2.5 to 4.5) than in the medically managed group (0.7; 95% CI, -0.8 to 2.2).

Section Summary: Severe Left Ventricular Dysfunction Considering Revascularization
Evidence for the use of PET to assess myocardial viability consists of a large randomized controlled trial that randomized patients with LV dysfunction into 2 groups: one was managed by physicians receiving PET images to inform care decisions, and the other was managed by physicians who did not receive PET images. Follow-up at 1 year and 5 years showed that when patients received care as indicated by the PET images, they were at decreased risk for cardiac death, myocardial infarction, or recurrent hospital stay compared with patients who did not. Available evidence from smaller trials has suggested that the accuracy of PET and SPECT are roughly similar for this purpose. PET may be more sensitive regarding small defects, but the clinical significance of identifying small defects is uncertain.

Myocardial Blood Flow Quantification
Several publications have described the use of PET imaging to quantify both MBF and myocardial flow reserve (MFR; defined as stress MBF/rest MBF).[21,22] However, as noted in an accompanying editorial[23] and by subsequent reviewers,[24] larger prospective clinical trials are needed to understand the clinical utility of these approaches.

Clinical Validity
In 2017, Hsu et al published a study comparing SPECT with N 13 ammonia PET in blood flow quantitation.[25] Healthy patients (n=12) and patients with CAD (n=16) underwent both SPECT and N 13 ammonia PET flow scans. MFR measures by SPECT and PET did not differ significantly in healthy patients. The MFR measures were also comparable in patients with CAD. The authors concluded that MFR can be accurately measured by either modality.

Stuijfzand et al (2015) used oxygen 15–labelled water PET imaging in 92 patients with 1-2 vessel disease to quantify MBF, MFR, and "relative flow reserve" (defined as stress MBF in a stenotic area/stress MBF in a normal perfused area).[26] Relative flow reserve was evaluated as a potential noninvasive alternative to FFR on coronary angiography. Using optimized cut points for PET detection of hemodynamically significant CAD (FFR as reference standard), area under the curve (AUC) analysis showed similar diagnostic performance for all 3 measures (0.76 [95% CI, 0.66 to 0.86] for MBF; 0.72 [95% CI, 0.61 to 0.83] for MFR; 0.82 [95% CI, 0.72 to 0.91] for relative flow reserve; p>0.05 for all comparisons).

Clinical Utility
Taqueti et al (2015) evaluated the association between MFR (called coronary flow reserve [CFR] in this study) and cardiovascular outcomes in 329 consecutive patients referred for invasive coronary angiography after stress PET perfusion imaging.[27] Patients with a history of CABG or heart failure, or with LVEF less than 40%, were excluded. Patients underwent Rb-82 or N 13 ammonia PET imaging and selective coronary angiography. MFR was calculated as the ratio of stress to rest MBF for the whole left ventricle. The primary outcome was a composite of cardiovascular death and hospitalization for heart failure. These outcomes were chosen because they are thought to be related to microvascular dysfunction, which impacts PET MBF measures, as opposed to obstructive CAD, which characteristically presents with myocardial infarction and/or revascularization. Patients were followed for a median of 3.1 years (interquartile range, 1.7-4.3) for the occurrence of MACE (comprising death, cardiovascular death, and hospitalization for heart failure or myocardial infarction). During follow-up, 64 (19%) patients met the primary composite end point. In a multivariate model that included pretest clinical score (to determine the pretest probability of obstructive, angiographic CAD), LVEF, left ventricular ischemia, early revascularization (within 90 days of PET imaging), and Coronary Artery Disease Prognostic Index, MFR was statistically associated with the primary outcome (hazard ratio [HR] per 1 unit decrease in continuous MFR score, 2.02; 95% CI, 1.20 to 3.40). The model used binary classification defined by median MFR; and the incidence of the primary outcome was 50% in patients with low or high CFR. A statistically significant interaction between CFR and early revascularization by CABG was observed: Event-free survival for patients with high CFR who underwent early revascularization was similar in groups who received CABG (n=17), percutaneous coronary intervention (n=72), or no revascularization (n=79); among patients with

low CFR who underwent early revascularization, event-free survival was significantly better in the CABG group (n=22) compared with the percutaneous coronary intervention group (n=85; p=0.006) and the no-revascularization group (n=57; p=0.001).

In 2011, Ziadi et al reported on a prospective study of the prognostic value of MFR with Rb-82 PET in 704 consecutive patients assessed for ischemia.[28] Ninety-six percent (n=677) of patients were followed for a median of 387 days; most (90%) were followed 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. The primary outcome was the prevalence of hard cardiac events (myocardial infarction and cardiac death); the secondary outcome was the prevalence of MACE (comprising cardiac death, myocardial infarction, later revascularization, and cardiac hospitalization). Patients with a normal summed stress score but 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 preserved MFR. Patients with abnormal summed stress score and impaired MFR had a higher incidence of hard events (11.4% vs 1.1%) and MACE (24% vs 9%) compared with patients who had preserved MFR. Rb-82 MFR was an independent predictor of cardiac hard events (HR=3.3) and MACE (HR=2.4) over summed stress score. Three (0.4%) patients were classified up and 0 were classified down with MFR in the multivariate model (p=0.092).

Murthy et al (2011) examined the prognostic value of Rb-82 PET MFR (called CFR in this study) in a retrospective series of 2783 patients referred for rest/stress PET myocardial perfusion imaging.[29] CFR was calculated as the ratio of stress to rest MBF using semi-quantitative PET interpretation. The 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 MFR to a multivariate model containing clinical covariates (e.g., CAD risk factors and CAD history) significantly improved model fit and improved the c index, a measure of discrimination performance, from 0.82 to 0.84 (p=0.02). MFR 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 MFR was observed in both diabetic and nondiabetic patients.[30]

Section Summary: Myocardial Blood Flow Quantification
Evidence is growing for the association of quantitative MBF and MFR with cardiovascular outcomes. Some but not all prospective studies have shown improvements over prognostic models based on clinical risk factors for cardiac events. Editorialists have commented on the potential utility of quantitative perfusion for understanding cardiac physiology and for informing future research.[31,32] However, because some studies used data-driven cut points and did not include healthy volunteers to verify discriminative ability (spectrum bias), these methods are considered to be in a developmental stage for clinical use.

Cardiac Sarcoidosis
Based on clinical input received in 2011, an additional indication for the workup of cardiac sarcoidosis was added to the evidence review. There is no standard diagnostic criterion for cardiac sarcoidosis. The latest consensus statement (2014) issued by the Heart Rhythm Society (HRS) stated that if a histologic diagnosis along with at least 1 clinical symptom (eg, reduced LVEF, heart block, patchy uptake of FDG-PET, late gadolinium enhancement on cardiac MRI, or cardiomyopathy) were present, the patient had a 50% or greater likelihood of cardiac sarcoidosis.[33] Currently, clinicians are combining clinical data with imaging techniques (cardiac MRI and FDG-PET) to make a diagnosis.

Clinical Validity
Systematic Reviews
In 2016, Tang et al published a systematic review on the overall diagnostic performance of FDG-PET/CT in cardiac sarcoidosis, and on subgroups based on the type of patient preparation methods (fasting time, heparin administration, diet).[34] The literature search, conducted through August 2014, identified 16 nonrandomized studies (total N=559 patients) for inclusion. Study

quality was assessed using QUADAS-2, with most studies having a low risk of bias. Overall sensitivity and specificity, when a large single study with a short fasting duration was excluded, were 81% (95% CI, 76% to 86%) and 82% (95% CI, 77% to 86%), respectively. Subgroup analyses based on the type of patient preparation method showed that the diagnostic odds ratio improved when patients fasted longer (≥12 hours) and heparin was administered. Placing the patient on a high-fat, low-carbohydrate diet before scanning did not affect the diagnostic accuracy of FDG-PET/CT.

A 2012 meta-analysis by Youssef et al identified 7 studies (total N=164 patients).[35] 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. The pooled sensitivity of PET by random-effects meta-analysis was 89%, and pooled specificity was 78%. The summary AUROC was 93%, suggesting a good level of diagnostic discrimination.

A 2009 review by Sharma reported that cardiac MRI was the more established imaging modality in diagnosing sarcoidosis, with an estimated sensitivity of 100% and specificity of 80%. Studies using FDG-PET showed high sensitivities; however, the population sizes of the studies were small. The reviewer asserted that imaging studies had incremental value when combined with clinical evaluation and/or myocardial biopsy in the diagnosis of cardiac sarcoidosis and called for additional research on the role of MRI and/or PET for this use.[36]

Nonrandomized Studies
In 2016, Lapa et al published a study to determine whether PET/CT using radiolabeled somatostatin receptor (SSRT) ligands for visualization of inflammation would accurately diagnose cardiac sarcoidosis.[37] Fifteen patients with sarcoidosis and suspicion of cardiac involvement underwent both SSTR-PET/CT and cardiac MRI. Concordant results between PET/CT and MRI occurred in 12 of the 15 patients.

In 2017, Dweck et al published a study evaluating the usefulness of a hybrid of cardiac MRI and FDG-PET to diagnose cardiac sarcoidosis.[38] Patients with suspected cardiac sarcoidosis (N=25) underwent FDG-PET imaging simultaneously with cardiac MRI. The investigators categorized 4 patient groups (MRI+/PET+, MRI+/PET-, MRI-/PET+, MRI-/PET-). The patients with MRI+/PET+ results had increased FDG activity that corresponded with the pattern of injury indicating active cardiac sarcoidosis. The remaining patients, with MRI+/PET-, MRI-/PET+, and MRI-/PET- results, did not show evidence of active cardiac sarcoidosis. Detecting active cardiac sarcoidosis, which is frequently subclinical, is beneficial so that anti-inflammatory therapy can be initiated. The authors concluded that simultaneous assessment of MRI and disease activity with PET permits a more accurate assessment of pattern of injury and disease activity in a single scan, which can impact therapeutic management.

Yokoyama et al (2015) conducted a study on 92 consecutive patients with suspected cardiac sarcoidosis. The patients underwent FDG-PET/CT following clinical assessment and imaging (electrocardiogram, echocardiography, MRI, perfusion scintigraphy) at the discretion of their physicians. The authors reported an AUC of 0.96 for identifying patients with cardiac sarcoidosis using optimized cut points for the maximum standardized uptake value on FDG-PET/CT.[39]

Clinical Utility
No studies evaluating the clinical utility of using PET or PET/CT in diagnosing cardiac sarcoidosis were identified.

Section Summary: Cardiac Sarcoidosis
Left untreated, cardiac sarcoidosis can lead to serious developments such as arrhythmia, heart failure, pericarditis, and heart attacks. However, there is no criterion standard for diagnosing cardiac sarcoidosis. A combination of clinical evaluations and results from imaging techniques are used in the clinician's assessment. Results from 2 meta-analyses have shown that PET can be a useful tool in this diagnostic process. Since the meta-analyses, small nonrandomized studies

have been published that evaluated variations in PET techniques such as using a radiolabeled SSRT ligand and adding a simultaneous cardiac MRI. These studies have shown positive results.

Summary of Evidence

For individuals with suspected coronary artery disease and an indeterminate SPECT scan who receive PET, the evidence includes several systematic reviews and meta-analyses. Relevant outcomes are test accuracy and disease-specific survival. Meta-analyses of studies in which PET results were compared with results from coronary angiography and fractional flow reserve have shown that PET is comparable in diagnostic accuracy to these referent standards. In meta-analyses of studies that included clinical outcomes such as mortality and adverse cardiac events, results have shown that PET is a useful prognostic tool. Subgroup analyses have shown that PET can be useful in patients whose body habitus is likely to result in indeterminate SPECT scans (e.g., patients with moderate to severe obesity). The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with left ventricular dysfunction who are potential candidates for revascularization who undergo cardiac PET scanning to assess myocardial viability, the evidence includes a large randomized controlled trial with long-term follow-up and several small trials comparing SPECT with PET. Relevant outcomes are test accuracy and morbid events. In the large randomized controlled trial, patients with left ventricular dysfunction were randomized to care from physicians who would make management decisions based on PET images to care from physicians who would make management decisions without PET images. At 1- and 5-year follow-ups, patients who received care indicated by the PET images were at decreased risk for cardiac death, myocardial infarction, and recurrent hospital stays compared with patients who did not. The trials comparing SPECT with PET showed that both modalities were useful in managing patients considering revascularization. Evidence-based recommendations from specialty societies have concluded that PET scanning is at least as good as, and likely superior, to SPECT scanning for this purpose. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with coronary artery disease who require myocardial blood flow quantification who receive quantitative cardiac PET, the evidence includes observational studies. The relevant outcome is morbid events. Studies adding PET-derived quantitative myocardial blood flow and myocardial flow reserve to prognostic models of clinical risk factors for cardiac events have reported inconsistent results, indicating that these methods are in a developmental stage for clinical use. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with suspected or diagnosed cardiac sarcoidosis who require evaluation who receive cardiac PET, the evidence includes systematic reviews and meta-analyses. The relevant outcome is test accuracy. Currently, there is no criterion standard for diagnosing cardiac sarcoidosis. A combination of clinical evaluations and results from imaging techniques, usually magnetic resonance imaging (MRI), are used during the clinician's assessment. The pooled results from meta-analyses have shown good sensitivity, specificity, and area under the curve estimates. Several small studies have evaluated variations in PET techniques such as using a radiolabeled somatostatin receptor ligand and adding a simultaneous cardiac MRI. Reported results were positive in these small studies, but larger samples are needed to confirm the usefulness of these changes. While MRI is the imaging technique most often used to evaluate cardiac sarcoidosis, for patients who are unable to undergo MRI (e.g., patients with a metal implant), evidence supports PET scanning as the preferred test. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

Supplemental Information

Clinical Input from Physician Specialty Societies and Academic Medical Centers

While the various physician specialty societies and academic medical centers may collaborate, and make recommendations during this process, through the provision of appropriate reviewers,

input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

Clinical input received by Blue Cross Blue Shield Association in 2011 was in general agreement with the medical necessity of positron emission tomography (PET) for myocardial viability or for patients with an indeterminate single-photon emission computed tomography (SPECT) scan. However, reviewers disagreed on using a strict body mass index cutoff to define patients in whom a SPECT scan would be expected to be suboptimal. Therefore, the language of the policy statement was changed to "Cardiac PET scanning may be considered medically necessary to assess myocardial perfusion and thus diagnose coronary artery disease in patients with indeterminate SPECT scan; or in patients for whom SPECT could be reasonably expected to be suboptimal in quality on the basis of body habitus."

Three Blue Cross Blue Shield Association reviewers responded to the question whether PET scanning was medically necessary for the workup of patients with suspected cardiac sarcoidosis. All three agreed that PET scanning was medically necessary for this patient group. Two of these reviewers indicated that magnetic resonance imaging (MRI) scanning was the preferred test in the workup of cardiac sarcoidosis but that PET scanning was medically necessary for patients who were unable to undergo MRI. As a result, an additional indication was added to the policy statement for workup of cardiac sarcoidosis: "Cardiac PET scanning may be considered medically necessary for the diagnosis of cardiac sarcoidosis in patients who are unable to undergo 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."

Practice Guidelines and Position Statements
American College of Cardiology
In 2003, the American College of Cardiology, American Heart Association, and American Society for Nuclear Cardiology updated their joint guidelines for cardiac radionuclide imaging, including cardiac applications of positron emission tomography (PET).[40] Table 6 summarizes the guidelines for PET and single-photon emission computed tomography (SPECT) imaging in patients with an intermediate risk of coronary artery disease (CAD).

Table 6. Guidelines for Positron Emission Tomography and Single-Photon Emission Computed Tomography in Patients with Intermediate Coronary Artery Disease Risk[40]

Indication	Class	
	SPECT	PET
Identify extent, severity, and location of ischemia (SPECT protocols vary according to whether patient can exercise)	I	IIa
Repeat test after 3-5 y 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 >20% 10-y risk of a coronary disease event) (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	Not appropriate	I

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

These guidelines concluded that PET "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)."[40] However, the guidelines indicated that either PET or SPECT scans are class I indications for predicting improvement in

regional and global left ventricular function and natural history after revascularization; therefore, the guidelines did not indicate a clear preference for PET or SPECT scans in this situation.

In 2009, the American College of Cardiology and American Heart Association collaborated with 6 other imaging societies to develop Appropriate Use Criteria for cardiac radionuclide imaging (RNI).[41] Their report stated:

> "...use of cardiac RNI for diagnosis and risk assessment in intermediate- and high-risk patients with coronary artery disease (CAD) was viewed favorably, while testing in low-risk patients, routine repeat testing, and general screenings in certain clinical scenarios were viewed less favorably. Additionally, use for perioperative testing was found to be inappropriate except for high selected groups of patients."

Canadian Cardiovascular Society et al

In 2007, Canadian Cardiovascular Society and 4 other Canadian imaging societies 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 another, equivocal test, eg, obesity (class I recommendation, level B evidence).[7]

American College of Radiology

The 2011 American College of Radiology (ACR) Appropriateness Criteria considered both SPECT and PET to be appropriate for the evaluation of patients with a high probability of CAD.[42] ACR indicated that PET perfusion imaging has advantages over SPECT, including higher spatial and temporal resolution. Routine performance of both PET and SPECT are unnecessary. The 2017 update[43] stated:

> "Hybrid PET scanners use CT [computed tomography] for attenuation correction (PET/CT) following completion of the PET study. By coupling the PET perfusion examination findings to a CCTA [coronary computed tomographic angiography], PET/CT permits the fusion of anatomic coronary arterial and functional (perfusion) myocardial information and enhances diagnostic accuracy. The fused examinations can accurately measure the atherosclerotic burden and identify the hemodynamic functional significance of coronary stenosis. The results of the combined examinations can more accurately identify patients for revascularization."

The 2012 ACR Appropriateness Criteria also recommended PET for the evaluation of patients with chronic chest pain and low-to-intermediate probability of CAD.[44]

ACR does not recommend PET for patients with acute nonspecific chest pain who have low probability of CAD[45] or for asymptomatic patients at risk for CAD.[46]

European Society of Cardiology

European Society of Cardiology published evidence-based consensus guidelines on the diagnosis and treatment of acute and chronic heart failure in 2012.[47] In 2016, the Society updated its guidelines, reaffirming the use of SPECT for assessment of ischemia and myocardial viability to consider suitability for coronary revascularization.[48] Additional revisions indicated that:

> "Echocardiography is the method of choice in patients with suspected heart failure, for reasons of accuracy, availability and safety... Gated SPECT can also yield information on ventricular volumes and function, but exposes the patient to ionizing radiation. Positron emission tomography (PET) (alone or with CT) may be used to assess ischemia and viability, but the flow tracers (N-13 ammonia or O-15 water) require an on-site cyclotron. Rubidium is an alternative tracer for ischemia testing with PET. Limitations include radiation exposure for PET imaging."

Japanese Society of Nuclear Cardiology

In 2014, the Japanese Society of Nuclear Cardiology published recommendations on PET for cardiac sarcoidosis.[49] In Japan, fluorine 18 fluorodeoxyglucose PET (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 Japanese Ministry of Health and Welfare 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 Recommendations
No U.S. Preventive Services Task Force recommendations for the use of PET in cardiac imaging have been identified.

Medicare National Coverage
Beginning 2002, Medicare began to cover FDG-PET for the determination of myocardial viability as a primary or initial diagnostic study before revascularization and continued to cover FDG-PET when used as a follow-up to an inconclusive SPECT.[50] However, if a patient only receives FDG-PET with inconclusive results, a follow-up SPECT is not covered. U.S. Food and Drug Administration (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 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."

Ongoing and Unpublished Clinical Trials
Some currently unpublished trials that might influence this review are listed in Table 7.

Table 7. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01288560	Alternative Imaging Modalities in Ischemic Heart Failure (AIMI-HF) Project I-A of Imaging Modalities to Assist with Guiding Therapy and the Evaluation of Patients with Heart Failure (IMAGE-HF)	1511	Sep 2017
NCT01434043	Diagnostic Accuracy of Cardiac CT Perfusion Compared to PET Imaging	30	Dec 2017
NCT01288560	Alternative Imaging Modalities in Ischemic Heart Failure (AIMI-HF) Project I-A of Imaging Modalities to Assist with Guiding Therapy and the Evaluation of Patients with Heart Failure (IMAGE-HF)	1511	Mar 2018
NCT00756379	Randomized Trial of Comprehensive Lifestyle Modifications, Optimal Pharmacological Treatment and PET Imaging for Detection and Management of Stable Coronary Artery Disease	1300	Jan 2019
NCT03103490	18F-FSPG PET/MRI Imaging of Cardiac Sarcoidosis or Inflammation	20	Apr 2020
Unpublished			
NCT01934985	Dynamic Cardiac SPECT Imaging	160	unknown
NCT01109992	Integrated Dual Exercise and Lexiscan PET: (IDEALPET)	41	Jun 2017 (completed)

NCT: national clinical trial.

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Documentation for Clinical Review

Please provide the following documentation (if/when requested):
- 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 product 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/IE
The following services may be considered medically necessary in certain instances and investigational in others. Services may be considered medically necessary when policy criteria are met. Services may be considered investigational when the policy criteria are not met or when the code describes application of a product in the position statement that is investigational.

Type	Code	Description
CPT®	0482T	Absolute quantitation of myocardial blood flow, positron emission tomography (PET), rest and stress (List separately in addition to code for primary procedure) *(Code effective 1/1/2018)*
	78459	Myocardial imaging, positron emission tomography (PET), metabolic evaluation
	78491	Myocardial imaging, positron emission tomography (PET), perfusion; single study at rest or stress
	78492	Myocardial imaging, positron emission tomography (PET), perfusion; multiple studies at rest and/or stress
HCPCS	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
ICD-10 Procedure	C23GKZZ	Positron Emission Tomographic (PET) Imaging of Myocardium using Fluorine 18 (F-18)

Type	Code	Description
	C23GMZZ	Positron Emission Tomographic (PET) Imaging of Myocardium using Oxygen 15 (O-15)
	C23GQZZ	Positron Emission Tomographic (PET) Imaging of Myocardium using Rubidium 82 (Rb-82)
	C23GRZZ	Positron Emission Tomographic (PET) Imaging of Myocardium using Nitrogen 13 (N-13)
	C23GYZZ	Positron Emission Tomographic (PET) Imaging of Myocardium using Other Radionuclide
	C23YYZZ	Positron Emission Tomographic (PET) Imaging of Heart using Other Radionuclide
ICD-10 Diagnosis	All Diagnoses	

Policy History

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

Effective Date	Action	Reason
12/15/2014	Policy title change from Positron Emission Tomography (PET) Policy revision with position change	Medical Policy Committee
01/01/2017	Policy revision without position change	Medical Policy Committee
11/01/2017	Policy revision without position change	Medical Policy Committee
01/01/2018	Coding update	Administrative Review

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 (as applicable to your plan)

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 be directed to the Prior Authorization Department. Please call (800) 541-6652 or visit the provider portal at www.blueshieldca.com/provider.

Disclaimer: This medical policy is a guide in evaluating the medical necessity of a particular service or treatment. Blue Shield of California may consider published peer-reviewed scientific literature, national guidelines, and local standards of practice in developing its medical policy. Federal and state law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over medical policy and must be considered first in determining covered services. Member contracts may differ in their benefits. Blue Shield reserves the right to review and update policies as appropriate.