



Louisiana

Beta Amyloid Imaging with Positron Emission Tomography (PET) for Alzheimer Disease

Policy # 00381

Original Effective Date: 11/04/2013

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Note: Dopamine Transporter Imaging With Single-Photon Emission Computed Tomography is addressed separately in medical policy 00496.

Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Company considers beta amyloid (A β) imaging with positron emission tomography (PET) to be **investigational**.*

Background/Overview

The diagnosis of Alzheimer disease (AD) is divided into 3 categories: possible, probable, and definite AD. A diagnosis of definite AD requires postmortem confirmation of AD pathology, including the presence of extracellular A β plaques and intraneuronal neurofibrillary tangles in the cerebral cortex. Probable AD dementia is diagnosed clinically when the patient meets core clinical criteria for dementia and has a typical clinical course for AD. A typical clinical course is defined as an insidious onset, with the initial and most prominent cognitive deficits being either amnesic or nonamnesic (e.g., language, visuospatial, or executive function deficits) and a history of progressively worsening cognition over time. A diagnosis of possible AD dementia is made when the patient meets the core clinical criteria for AD dementia but has an atypical course or an etiologically mixed presentation.

Mild cognitive impairment (MCI) may be diagnosed when there is a change in cognition, but impairment is insufficient for the diagnosis of dementia. Features of MCI are evidence of impairment in 1 or more cognitive domains and preservation of independence in functional abilities. In some patients, MCI may be a prodementia phase of AD. Patients with MCI may undergo ancillary testing (e.g., neuroimaging, laboratory studies, neuropsychological assessment) to rule out vascular, traumatic, and medical causes of cognitive decline and to evaluate genetic factors. Because clinical diagnosis can be difficult, particularly early in the course of disease, there has been considerable interest in developing biomarkers for AD. One biomarker being evaluated is A β plaque density in the brain detected in vivo by PET. However, A β is present in individuals without dementia, in patients with mild or subjective cognitive impairment who may or may not progress to dementia, and in patients with other types of dementia, and may be absent in a substantial proportion of patients with clinical features of AD.

PET images biochemical and physiologic functions by measuring concentrations of positron-emitting chemicals in the body region of interest. Radiopharmaceuticals used for A β imaging may be generated in a cyclotron or nuclear generator and introduced into the body by intravenous injection. A number of carbon 11

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(¹¹C)- and fluorine 18 (¹⁸F)-labeled PET radiopharmaceuticals have been investigated for imaging brain A β .⁶

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)

In 2012, florbetapir F18 (Amyvid™[±]; Avid Radiopharmaceuticals [a subsidiary of Eli Lilly], Philadelphia, PA) was approved by the U.S. FDA through the premarket approval process as a radioactive agent for visualizing amyloid plaque in the brain. The FDA document prepared for the advisory committee meeting indicated that although florbetapir may detect pathology, there could be no claim of disease detection, because A β aggregates can be found in cognitively normal elderly patients as well as patients with AD.

In October 2013 and March 2014, FDA approved 2 other radioactive diagnostic imaging agents for detecting A β plaque: flutemetamol F18 (Vizamyl™[±]; GE Healthcare) and florbetaben F18 (Neuraceq™[±]; Piramal Life Sciences, Matran, Switzerland), respectively.

Amyvid, Vizamyl, and Neuraceq are indicated “for PET imaging of the brain to estimate A β neuritic plaque density in adult patients with cognitive impairment who are being evaluated for AD and other causes of cognitive decline. Prescribing information for all 3 agents states:

- The objective of A β image interpretation “is to estimate beta-amyloid neuritic plaque density in brain gray matter, not to make a clinical diagnosis.”
- A positive A β scan “does not establish the diagnosis of AD or other cognitive disorder.”
- A negative A β scan “indicates sparse to no neuritic plaques, and is inconsistent with a neuropathologic diagnosis of AD at the time of image acquisition; a negative scan result reduces the likelihood that a patient’s cognitive impairment is due to AD.”
- Florbetapir, florbetaben, and flutemetamol are not intended for use in “predicting development of dementia or other neurological condition” or for “monitoring responses to therapies.”

Centers for Medicare and Medicaid Services (CMS)

In September 2013, the CMS issued a national coverage determination through coverage with evidence development (CED), under §1862(a)(1)(E) of the Act, that provides limited coverage for the use of A β PET imaging in 2 scenarios: (1) clinically difficult differential diagnoses, such as AD versus frontotemporal dementia, when the use of A β PET imaging may improve health outcomes and the patient is enrolled in an approved clinical study, and (2) to enrich CMS-approved clinical trials of treatments or prevention strategies for AD. CMS will cover 1 A β PET scan per patient in clinical studies that meet prespecified criteria.

Rationale/Source

Studies of diagnostic tests can be divided into categories. Different schemes have been proposed. In this evidence review, we use the following categorization: (1) technical performance; (2) diagnostic accuracy (sensitivity, specificity, positive and negative predictive values) in relevant populations of patients, such as those who have MCI or suspected AD; and (3) effect on patient outcomes (i.e., demonstration that the diagnostic information can be used to improve patient outcomes).

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The criterion standard for the diagnosis of AD is postmortem neuropathologic examination. In the absence of comparisons with the criterion standard, long-term clinical follow-up (e.g., conversion from MCI to probable AD) may be used as a surrogate end point to evaluate the diagnostic performance of A β imaging with PET.

A β imaging may be particularly helpful for the future study of novel therapeutic agents that target amyloid plaques. However, the current clinical purposes of testing for A β plaque density would be to improve diagnostic accuracy (e.g., rule out AD) or predict conversion from MCI to AD. In general, evidence of a health benefit or clinical utility from testing requires demonstration that:

- incremental improvements in diagnostic or prognostic accuracy over current practice occur, *and*
- incremental improvements lead to improved health outcomes (e.g., by informing clinical management decisions), *and*
- these outcomes may be obtained (i.e., are generalizable) outside of the investigational setting.

A β Imaging With PET for Suspected AD

A 2013 Technology Evaluation Center (TEC) Assessment concluded that A β imaging with PET to evaluate suspected AD and other causes of cognitive decline does not meet the TEC criteria, based on a lack of direct evidence for clinical utility. The following is a summary of the main conclusions of the TEC Assessment:

“Studies have shown that florbetapir F18 PET results correlate with histopathologic findings at autopsy. This finding is important. Studies also have suggested that florbetapir F18 PET has some ability to differentiate between cognitively normal adults and patients with AD. However, the studies are limited by small sample sizes, differences in determining outcomes (e.g., qualitative versus quantitative, unknown impact of training for physicians inexperienced with this modality), and the lack of evidence obtained from populations encountered in clinical practice. No information is available on the impact of this test on clinical outcomes, and few data are available on whether it can accurately identify patients with MCI who will develop AD.”

Technical Performance

Evidence on technical performance of A β imaging for AD should demonstrate that the test measures what it is intended to measure (i.e., A β plaque). The best evidence on this would be direct comparison with a criterion standard test (histopathologic examination) for measuring amyloid plaque. Other important measures of technical performance are the reliability of testing, including both test-retest reliability and interobserver reliability in reading test results.

Florbetapir

In 2012, Clark et al published an extension of their pivotal study submitted to the U.S. FDA for the marketing application of florbetapir. This study reported on 59 participants with cognitive status ranging from normal to advanced dementia. Twelve participants had no cognitive impairment, 5 had MCI not meeting the criteria for dementia, 29 had AD, and 13 had other forms of dementia. All patients had direct measurement of amyloid burden by histopathologic examination, and images were interpreted by 3 readers using

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semiquantitative visual analysis on a scale from 0 to 4; median semiquantitative rating was used. A significant correlation of 0.76 and 0.79 was found between amyloid burden in the brain measured by florbetapir and the criterion standard of histopathology in patients who had an autopsy performed within 2 years and 12 months of imaging, respectively. This report added additional participants to those reported in the 2011 study (described next).

Data on technical performance of the test was included in a florbetapir pivotal study published in 2011. This study was a phase 3 multicenter trial with 2 separate cohorts. These cohorts were an autopsy cohort and a young, cognitively intact cohort. The autopsy cohort was drawn from 152 patients who had a projected life expectancy of 6 months or less. Thirty-five patients died and were autopsied within 12 months of PET imaging; 29 were included in the primary efficacy analysis. This cohort comprised 9 (31%) patients who were not cognitively impaired, 2 (7%) who were mildly impaired, 13 (45%) with a clinical diagnosis of AD, and 5 (17%) with a clinical diagnosis of a non-AD dementia.

All patients had direct measurement of amyloid burden by histopathologic examination, and 52% met pathologic criteria for AD. A significant correlation (0.78) was found between amyloid burden in the brain measured by Amyvid and histopathology; however, there was not an exact match between the 2 measures. The correlation between quantitative whole-brain florbetapir image scores and postmortem silver stain was 0.71. In a specificity cohort to evaluate false positives, the primary efficacy end point was the exclusion of amyloid on PET scans of 47 young controls who were negative for the apolipoprotein E ϵ 4 (*APOE4*) allele, randomly interspersed with PET scans of 40 patients in the autopsy cohort. The study achieved a specificity of 100% in this cohort, although it was noted that the young controls were outside of the intended use population.

Reproducibility of the readings was assessed using 3 trained readers blinded to clinical information. Using a binary scale (positive or negative for amyloid), sensitivity ranged from 55% to 90% for the 3 readers, and in 24% to 45% of the images (depending on the sample), at least 1 reader would have had a different interpretation of amyloid status from the other readers. Subsequent reanalysis for publication used the majority rating of 3 nuclear medicine physicians as the primary outcome variable, resulting in 96% agreement between PET images using fluorine 18 (^{18}F ; florbetapir) and histopathologic results in the 29 patients in the primary analysis cohort.

Siderowf et al (2014) compared patterns of amyloid deposition by florbetapir PET imaging in 31 patients with probable AD (n=10), probable dementia with Lewy bodies (n=11), or probable Parkinson disease (n=5), and 5 healthy controls. Diagnoses were made by research criteria. PET images were read by 5 readers blinded to clinical data; the majority interpretation was used for analysis. Interrater agreement was high ($\kappa=0.88$; 95% confidence interval [CI], 0.77 to 0.99). Differences in the standardized uptake value ratio (SUVR) between healthy controls and patients with AD, and between patients with Parkinson disease and patients with AD, were statistically significant. Differences in SUVR between patients with Lewy body dementia and patients with AD were statistically significant in only 2 of 6 brain regions imaged. However, statistical analyses were not corrected for multiple comparisons. This study also had a small sample size and lacked histopathologic confirmation of probable dementia diagnoses.

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Florbetaben

Information about a pivotal florbetaben study is provided in the prescribing information. Reliability and reproducibility of image interpretation were evaluated using 5 new readers and images from 273 patients and 188 healthy controls enrolled in previous studies. Patients had AD (67%), MCI (19%), other dementias (13%), or Parkinson disease (2%). Median age of all 461 enrollees was 72 years (range, 22-98 years); 43% were female; 78% were white. Readers were trained by electronic media rather than in-person. Interreader agreement was high across scans from all patients ($\kappa=0.80$; 95% CI, 0.77 to 0.83) and for scans from 54 patients who underwent postmortem autopsy ($\kappa=0.75$; 95% CI, 0.67 to 0.83). Intrareader reproducibility for 46 images ranged from 91% to 98% across the 5 readers.

In 2015, Sabri et al published an international, phase 3, histopathologic study of florbetaben-PET for detecting neuritic A β plaque (N=218). Patients with clinical diagnoses of AD, dementia with Lewy bodies, or other dementias; patients without dementia (primarily with oncologic disorders); and a cohort of young (age, 22-38 years), cognitively normal healthy volunteers considered highly likely to be A β -negative (n=11) were included. The optimal thresholds for sensitivity and specificity for detecting A β were determined by quantitative SUVR receiver operating characteristic (ROC) curve analysis. At the time of data analysis, 74 (36%) of 207 patients had died (57 with AD, 3 with Lewy body dementia, 6 with other dementias, 8 without dementia; mean age, 80 years). Mean time from PET scan to death was 329 days. At autopsy, A β was present in 44 (77%) of 57 patients diagnosed clinically with AD, 1 (33%) of 3 patients with Lewy body dementia, 1 (17%) of 6 patients with other dementias, and 1 (13%) of 8 patients without dementia. Forty-six of 47 neuritic A β -positive cases were read as florbetaben-PET positive, and 24 of 27 neuritic A β -negative cases were read as PET negative (sensitivity, 98%; 95% CI, 94% to 100%; specificity, 89%; 95% CI, 77% to 100%). Interrater agreement was high ($\kappa=0.90$; 95% CI, 0.81 to 0.98). Using an optimized quantitative SUVR threshold, sensitivity was 89% (95% CI, 81% to 98%) and specificity was 92% (95% CI, 82% to 100%).

Flutemetamol

In 2015, Curtis et al published an international, phase 3, histopathologic, pivotal study of flutemetamol-PET for detecting neuritic A β plaque (N=203). Patients with AD, other dementia, unspecified memory loss, or no cognitive impairment who were 55 years or older and terminally ill with a life expectancy of 1 year or less were included. PET images were read by 4 nuclear medicine physicians and 1 radiologist using a majority-read approach. Of 69 patients who died during the study (mean age, 81 years), 43 (63%) brains were A β -positive and 25 (37%) were A β -negative by histopathology (1 brain was not evaluated). Flutemetamol-PET imaging was performed a mean of 3.5 months (range, 0-13 months) before death. Median sensitivity of flutemetamol PET imaging for A β was 88%, and median specificity was 88%. Interrater and intrarater agreement was high (Fleiss $\kappa=0.72$, Cohen κ range, 0.60-1.00 across raters, respectively). The study lacked MCI patients and used majority rating for image interpretation.

¹⁸F-Labeled A β Tracers

For all 3 A β radioactive tracers, FDA has reported correlations between A β in PET scans and in histopathology specimens of 0.68 (95% CI, 0.43 to 0.82) to 0.76 (95% CI, 0.56 to 0.87) across brain regions.

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In 2013, Vandenberghe et al summarized published studies on test-retest variability and interrater reliability of all 3 tracers. As shown in Table 1, variability in repeat testing was low for each agent, and interrater reliability (κ) varied from 0.6 to 0.96. Because values listed in Table 1 were derived from heterogeneous studies, cross-tracer comparisons are indirect.

Table 1. Indirect Comparison of β -Amyloid PET Scan Reproducibility¹⁹

Outcomes	Florbetapir	Florbetaben	Flutemetamol
Mean (SD) test-retest variability of SUVR, ^a %	2.4 (1.4)	6.2 (range, 0.6-12.2)	1.5 (0.7)
Interrater consistency of binary readings, ^b κ	0.58-0.76	0.60	0.96

PET: positron emission tomography; SUVR: standardized uptake value ratio using cerebellum as reference region.

^a In patients with Alzheimer dementia scanned within 1 month from clinical diagnosis.

^b Positive or negative.

Use of SUVR has been shown to decrease interreader variability of florbetapir PET scan interpretation ($\kappa=0.92$) compared to qualitatively read studies ($\kappa=0.69$). However, as Minoshima noted in an accompanying editorial, if cases have differing impressions between qualitative interpretation and quantitative assessment, it is not known which is more accurate.

Section Summary: Technical Performance

Evidence on technical performance is mainly from pivotal studies. A strength of the florbetapir pivotal study and the phase 3 studies of florbetaben and flutemetamol was the comparison of imaging with the criterion standard of postmortem histopathology. Limitations of the florbetapir study included small sample size, a majority rating for assessing diagnostic accuracy, and having only 2 patients in the MCI category, which is the population for whom the test is most likely to be used. Similarly, the florbetaben and flutemetamol studies did not include patients with MCI. Evidence from these studies has indicated that agreement between histopathology and A β testing by PET is good but not perfect. There is evidence for interobserver variability in reading the test; using a majority of 2 of 3 readers leads to a high agreement with histopathology. A summary review and prescribing information have indicated that test-retest variability is low while interrater reliability is sufficient.

Diagnostic Accuracy

The lack of a criterion standard for the diagnosis of AD for use in living patients is a barrier to high-quality research. The highest quality studies of diagnostic accuracy are those that use pathologic examination of brain tissue in deceased patients and include a population of patients with AD, MCI, other neurologic disorders, and patients without neurologic disease. The main limitation in these studies is the patient population, which is not representative of the population for which the test is intended.

A 2016 systematic review and meta-analysis by Morris et al pooled sensitivity and specificity estimates from 9 studies for both visual and quantitative assessment of A β testing by PET with florbetapir, florbetaben, and flutemetamol. For the 5 studies that reported visual assessment PET images and included patients with MCI along with AD and healthy controls, sensitivity was 93% (95% CI, 87% to 96%) and specificity was 66% (95% CI, 52% to 77%). Specificity was lower than the pooled estimate, which did not include patients

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with MCI (85%). Quantitative analysis was reported for 4 studies that included patients with MCI and AD along with healthy controls; pooled sensitivity was 94% (95% CI, 88% to 97%) and specificity was 79% (95% CI, 62% to 89%).

The first study that used the criterion standard postmortem histopathology as the reference standard was the 2011 pivotal study by Clark et al that reported on the diagnostic accuracy of florbetapir. The extension study used majority consensus of 5 independent reviewers rating the images on a binary scale of amyloid-positive or -negative as the final test reading. Sensitivity and specificity were calculated in comparison with the criterion standard of histopathology. In 46 participants with a scan-to-autopsy time of less than 12 months, sensitivity, specificity, and accuracy were 96% (80%-100%), 100% (78%-100%), and 98% (87%-100%), respectively. For those with a scan-to-autopsy time of less than 2 years, sensitivity, specificity, and accuracy were 92% (78%-98%), 100% (78%-100%), and 95% (85%-99%), respectively.

The pivotal study used a majority consensus of 3 independent reviewers as the final test reading; sensitivity and specificity were calculated in comparison with the criterion standard of histopathology. Of 15 patients who met pathologic criteria for AD, 14 had positive florbetapir scans (sensitivity, 93%). Of 14 patients who did not meet pathologic criteria for AD, all 14 had negative scans (specificity, 100%). Scans from all young patients (27 APOE4+ and 47 APOE-) were negative. Exploratory analysis indicated that in 3 (20%) patients, clinical diagnosis did not match final autopsy diagnosis.

Another study that used autopsy as the criterion standard for diagnosis was the pivotal cohort study of flutemetamol. This study assessed diagnostic accuracy and reproducibility (both intra- and interreader) of flutemetamol PET imaging. In 68 patients 55 years of age or older who died within 13 months of imaging, clinical diagnoses were AD in 30 (44%) patients, other cognitive disorders in 17 (25%) patients, and no cognitive impairment in 21 (31%) patients. Five readers blinded to clinical information interpreted PET images independently and in random order. The criterion standard was postmortem brain amyloid density: 43 (63%) were positive on histopathology review, and 25 (37%) were negative. Adequate sensitivity was defined as a lower bound of the 95% CI for sensitivity above 70% for at least 3 of the 5 readers. This criterion was met; median sensitivity was 88% (range, 81%-93%). Specificity, a secondary outcome, ranged from 44% to 92% with lower and upper 95% CI bounds ranging from 24% to 74% and 65% to 99%, respectively. Median specificity across the 5 readers was 88%. Interreader reproducibility met a prespecified minimum threshold of 0.6 for the lower 95% CI bound for the κ statistic ($\kappa=0.80$; 95% CI, 0.79 to 0.86). Intrareader reproducibility on 29 duplicate images was high.

There was also a study using a pathologic criterion standard that evaluated the tracer florbetaben. This study evaluated 205 (69%) patients who had AD, other non-AD dementia (15%), dementia with Lewy bodies (2%), or no clinical evidence of dementia (16%). Median patient age was 79 years (range, 48-98 years); 48% were female. Three trained readers, masked to clinical information, interpreted florbetaben PET images, which were then compared with postmortem histopathology in patients who died during the study (n=82). In most patients (55%), PET images were obtained less than 1 year before death. At autopsy, 30 (37%) patients had 5 or fewer A β plaques by silver stain and were considered negative; 52 (63%) patients had more than 5 plaques and were considered positive. Median sensitivity across readers was

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98% (range, 96%-98%), and median specificity was 80% (range, 77%-83%). In a subsequent study of images from the same 82 patients, 5 readers underwent electronic rather than in-person reader training. Median sensitivity across readers decreased to 96% (range, 90%-100%), as did median specificity, to 77% (range, 47%-80%).

Other studies have used the clinical diagnosis of AD as the criterion standard, and therefore have enrolled patients similar to those seen in clinical care. A 2011 industry-funded multicenter study by Fleisher et al pooled data from 4 phase 1 and 2 trials of florbetapir PET imaging for a total of 210 participants, including 68 patients with probable AD, 60 patients with MCI; and 82 older unimpaired controls. Quantitative SUVR thresholds were determined from the phase 3 trial previously described. Although there were significant differences in mean SUVRs across groups, there was considerable overlap in the range of values. The percentages of patients meeting threshold levels of amyloid with clinical AD, MCI, and cognitively healthy controls were 80.9%, 40.0%, and 20.7%, respectively. The percentage of patients with any identifiable florbetapir signal was 85.3%, 46.6%, and 28.1%, respectively. Among healthy controls, the percentage of patients with any florbetapir positivity increased linearly by age, ranging from 11.8% for patients 55 to 60 years of age to 41.7% for patients 81 years of age or older. *APOE4* carriers in the control group had approximately twice the percentage of florbetapir positivity as noncarriers, although this comparison was not statistically significant.

In 2012, Camus et al reported on the diagnostic performance of florbetapir PET scanning in a clinical setting. Included were 13 patients with AD, 12 with MCI, and 21 older unimpaired controls. PET images were assessed visually by 2 readers who were blinded to clinical information and quantitatively by the SUVR of cortical regions compared with the cerebellum. Sensitivity and specificity were calculated based on clinical diagnosis as the comparison standard. Agreement in visual analysis between the 2 readers yielded a κ value of 0.71. Comparing visual assessment with initial clinical diagnosis, 11 (85%) of 13 AD patients, 6 (50%) patients with MCI, and 13 (60%) of 21 control patients had positive scans, resulting in a sensitivity of 84.6% and specificity of 38.1% for discriminating AD patients from controls. A quantitative assessment of the global cortex SUVR showed a sensitivity of 92.3% and specificity of 90.5% at a cutoff value of 1.12 (ROCs area under the curve, 0.894). This study had a small sample size, used clinical diagnosis as a reference standard, and reported a high number of false positives with visual assessment of the images. In addition, quantitative analysis did not differentiate patients with MCI from unimpaired controls.

In a follow-up to an earlier study, Doraiswamy et al (2014) compared cognitive decline in 47 patients with MCI who were $A\beta$ -positive or $A\beta$ -negative by florbetapir PET imaging. Over 36 months of follow-up, 6 (35%) of 17 $A\beta$ -positive patients and 3 (10%) of 30 $A\beta$ -negative patients advanced to a diagnosis of AD or clinically significant worsening (defined as a 4-point decline on the 11-item Alzheimer Disease Assessment Scale, $p=0.054$). Sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for these outcomes combined were 67%, 71%, 35%, and 90%, respectively. This study had a small sample size, used a composite outcome, and lacked histopathologic confirmation of AD diagnoses.

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In a study of 201 physicians who treated patients with probable AD (n=121) or healthy controls (n=80), Schipke et al (2012) reported sensitivity, specificity, PPV, and NPV of florbetaben PET imaging of 82%, 83%, 47%, and 75%, respectively.

Ong et al (2013) compared florbetaben PET SUVR (referenced to the cerebellar cortex) in 45 patients with MCI and a separate cohort of 15 patients with AD. Mean (SD) SUVR across 6 brain regions imaged was statistically higher in patients with AD compared with patients who had MCI (1.96 [0.27] vs 1.54 [0.27]; $p < 0.05$). All patients with AD (100%) and 24 (53%) of 45 patients with MCI had high A β , defined by a cutoff value for mean SUVR of 1.45 or greater. Sensitivity, specificity, PPV, and NPV for discriminating AD from MCI were 100%, 47%, 38%, and 100%, respectively. This study was small, did not correct for multiple comparisons, and lacked histopathologic confirmation of AD diagnoses. In 2- and 4-year follow-ups of the MCI cohort (n=45), Ong et al (2015) reported that 18 (75%) of 24 patients with baseline A β -positive PET scans (by semiquantitative SUVR interpretation) progressed to AD within 2 years compared with 2 (10%) of 21 patients with baseline A β -negative PET scans. PPV and NPV for progression to AD at 2 years were approximately 76% and 91% to 95%, respectively, depending on method of image interpretation (semiquantitative vs visual read). At 4 years, 21 (88%) of 24 patients with baseline A β -positive PET scans had AD, and 5 (24%) of 21 patients with baseline A β -negative PET scans had developed a non-AD form of dementia. As in the original study, histopathologic confirmation of AD diagnoses was lacking.

Section Summary: Diagnostic Accuracy

Evidence on the diagnostic performance of A β testing is limited, and available studies have methodologic issues (e.g., small patient samples) that limit the validity of reported results. Some evidence has suggested that there are a high number of false-positive results in patients without AD. However, the pivotal study reported high specificity, so the true rate of false positives is uncertain. Further high-quality studies using populations of patients that represent those presenting in clinical care are needed to better define the diagnostic performance of this test.

Effect on Patient Outcomes

No trials have been identified that reported health outcomes after A β PET imaging, thus there is no direct evidence for clinical utility.

Possible clinical uses of A β testing could include confirming the diagnosis of AD to begin medications at an earlier stage, or ruling out AD, which could lead to further diagnostic testing to determine the etiology of dementia and/or avoidance of anti-Alzheimer medications that would be unnecessary.

Because the sensitivity and specificity of A β testing has not yet been established, it is not possible to determine an indirect chain of evidence that would indicate that health outcomes are improved. Because A β is present in elderly patients who do not have AD, it is unlikely that the test would have a high PPV, and, therefore it may have limited utility in confirming AD. It is possible that the NPV of testing could be high and that the test might be useful in ruling out AD. If true, it is uncertain how many patients would benefit from additional testing to determine etiology, or whether a substantial number of patients would avoid unnecessary medications that would otherwise be given.

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Section Summary: Effect on Patient Outcomes

Evidence on clinical utility (i.e., that health outcomes are improved by testing) is lacking. There are no studies that report on clinical outcomes after testing. Diagnostic accuracy of testing is too uncertain to determine whether testing is likely to impact management and/or lead to improved outcomes.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 2.

Table 2. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Ongoing			
NCT01886820 ^a	A Phase 3 Clinical Trial to Evaluate the Efficacy and Safety of [18F]NAV4694 PET for Detection of Cerebral Beta-Amyloid When Compared With Postmortem Histopathology	290	Dec 2017
NCT01518374 ^a	Clinical Evaluation of Florbetapir F 18 (18F-AV-45)	1800	Dec 2017
NCT02420756	Imaging Dementia—Evidence for Amyloid Scanning (IDEAS) Study: A Coverage With Evidence Development Longitudinal Cohort Study	18,488	Dec 2018
NCT02008357 ^a	Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease (A4 Study)	1150	Apr 2020
NCT02317250	Early and Long-Term Health Outcomes of Molecular Cerebral Imaging in Incipient Dementia (MCI-ID) II	1500	Dec 2020
Unpublished			
NCT01703702 ^a	A Randomized, Multicenter, Multicountry Study to Evaluate the Effectiveness of Florbetapir (18F) PET Imaging in Changing Patient Management and to Evaluate the Relationship Between Florbetapir (18F) PET Scan Status and Cognitive Decline	618	Apr 2015 (completed)

NCT: national clinical trial.

^a Denotes industry-sponsored or cosponsored trial.

Summary of Evidence

For individuals who have suspected AD who receive A β imaging with PET, the evidence includes pivotal studies for 3 agents. Relevant outcomes are test accuracy, other test performance measures, functional outcomes, and medication use. Literature on the use of A β PET to aid in the diagnosis of patients with suspected AD is limited. A pivotal phase 3 trial with florbetapir, although to be commended for its use of the criterion standard (histopathology), had a number of limitations including small sample size, use of a majority rating of 3 physicians, and very few patients in the mildly impaired category. The pivotal florbetaben and flutemetamol studies did not include patients with MCI. The sensitivity and specificity of A β imaging with PET have not yet been adequately determined in an appropriate population, including a larger number of patients with MCI. In addition, direct or indirect evidence of improved health outcomes with this technology is lacking. A β imaging with PET is not likely to help confirm AD in patients who present with cognitive impairment. It may have a role in ruling out AD in patients with MCI, but the diagnostic accuracy of testing in patients with MCI is too uncertain to determine whether testing is likely to impact management

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and/or lead to improved outcomes.. The evidence is insufficient to determine the effects of the technology on health outcomes.

References

1. Blue Cross and Blue Shield Association, Medical Policy Reference Manual, "Beta Amyloid Imaging with Positron Emission Tomography (PET) for Alzheimer's Disease", 6.01.55, 9:2016.
2. McKhann GM, Knopman DS, Chertkow H, et al. The diagnosis of dementia due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. May 2011;7(3):263-269. PMID 21514250
3. Hyman BT, Phelps CH, Beach TG, et al. National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease. *Alzheimers Dement*. Jan 2012;8(1):1-13. PMID 22265587
4. Albert MS, DeKosky ST, Dickson D, et al. The diagnosis of mild cognitive impairment due to Alzheimer's disease: recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement*. May 2011;7(3):270-279. PMID 21514249
5. Ossenkoppele R, Jansen WJ, Rabinovici GD, et al. Prevalence of amyloid PET positivity in dementia syndromes: a meta-analysis. *JAMA*. May 19 2015;313(19):1939-1949. PMID 25988463
6. Jansen WJ, Ossenkoppele R, Knol DL, et al. Prevalence of cerebral amyloid pathology in persons without dementia: a meta-analysis. *JAMA*. May 19 2015;313(19):1924-1938. PMID 25988462
7. Vallabhajosula S. Positron emission tomography radiopharmaceuticals for imaging brain Beta-amyloid. *Semin Nucl Med*. Jul 2011;41(4):283-299. PMID 21624562
8. U.S. Food and Drug Administration. FDA Advisory Committee briefing document: Peripheral and central nervous system drugs advisory committee. 2011; http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/PeripheralandCentralNervousSystemDrugsAdvisoryCommittee/UCM240265.pdf?utm_campaign=Google2&utm_source=fdaSearch&utm_medium=website&utm_term=amyvid&utm_content=5.
9. Eli Lilly and Company. Amyvid™ (florbetapir F18 injection) for intravenous use prescribing information, December 2013. <http://pi.lilly.com/us/amyvid-uspi.pdf>.
10. GE Healthcare. Vizamy™ (flutemetamol F18) injection prescribing information, October 2013. http://www3.gehealthcare.com/en/products/categories/nuclear_imaging_agents/vizamy.
11. Piramal Imaging. Neuraceq (florbetaben F 18 injection) for intravenous use prescribing information, 04/2014. http://piramal.com/neuraceq/images/Neuraceq_PI_031814.pdf.
12. Lijmer JG, Leeflang M, Bossuyt PM. Proposals for a phased evaluation of medical tests. *Med Decis Making*. Sep-Oct 2009;29(5):E13-21. PMID 19605881
13. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Beta Amyloid Imaging with Positron Emission Tomography (PET) for Evaluation of Suspected Alzheimer's Disease or Other Causes of Cognitive Decline. TEC Assessments. 2013;Volume 27:Tab 5.
14. Clark CM, Pontecorvo MJ, Beach TG, et al. Cerebral PET with florbetapir compared with neuropathology at autopsy for detection of neuritic amyloid-beta plaques: a prospective cohort study. *Lancet Neurol*. Aug 2012;11(8):669-678. PMID 22749065
15. Clark CM, Schneider JA, Bedell BJ, et al. Use of florbetapir-PET for imaging beta-amyloid pathology. *JAMA*. Jan 19 2011;305(3):275-283. PMID 21245183
16. Siderowf A, Pontecorvo MJ, Shill HA, et al. PET imaging of amyloid with Florbetapir F 18 and PET imaging of dopamine degeneration with 18F-AV-133 (florbenazine) in patients with Alzheimer's disease and Lewy body disorders. *BMC Neurol*. Apr 9 2014;14(1):79. PMID 24716655
17. Sabri O, Sabbagh MN, Seibyl J, et al. Florbetaben PET imaging to detect amyloid beta plaques in Alzheimer's disease: phase 3 study. *Alzheimers Dement*. Aug 2015;11(8):964-974. PMID 25824567
18. Curtis C, Gamez JE, Singh U, et al. Phase 3 trial of flutemetamol labeled with radioactive fluorine 18 imaging and neuritic plaque density. *JAMA Neurol*. Mar 2015;72(3):287-294. PMID 25622185
19. U.S. Food and Drug Administration. Neuraceq (florbetaben F18) injection summary review, 02/28/2014. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2014/204677Orig1s000TOC.cfm.
20. Vandenberghe R, Adamczuk K, Dupont P, et al. Amyloid PET in clinical practice: Its place in the multidimensional space of Alzheimer's disease. *Neuroimage Clin*. 2013;2:497-511. PMID 24179802

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21. Nayate AP, Dubroff JG, Schmitt JE, et al. Use of standardized uptake value ratios decreases interreader variability of [18F] Florbetapir PET brain scan interpretation. *AJNR Am J Neuroradiol.* Mar 12 2015. PMID 25767185
22. Minoshima S. Establishing amyloid PET imaging biomarkers: ongoing efforts {editorial}. *AJNR Am J Neuroradiol.* Jul 2015;36(7):1245-1246. PMID 25999415
23. Morris E, Chalkidou A, Hammers A, et al. Diagnostic accuracy of (18)F amyloid PET tracers for the diagnosis of Alzheimer's disease: a systematic review and meta-analysis. *Eur J Nucl Med Mol Imaging.* Feb 2016;43(2):374-385. PMID 26613792
24. U.S. Food and Drug Administration. Vizamy (flutemetamol F 18) summary review, 09/16/13. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/203137_vizamy_toc.cfm.
25. Fleisher AS, Chen K, Liu X, et al. Using positron emission tomography and florbetapir F18 to image cortical amyloid in patients with mild cognitive impairment or dementia due to Alzheimer disease. *Arch Neurol.* Nov 2011;68(11):1404-1411. PMID 21747008
26. Camus V, Payoux P, Barre L, et al. Using PET with 18F-AV-45 (florbetapir) to quantify brain amyloid load in a clinical environment. *Eur J Nucl Med Mol Imaging.* Apr 2012;39(4):621-631. PMID 22252372
27. Johnson KA, Sperling RA, Gidicsin CM, et al. Florbetapir (F18-AV-45) PET to assess amyloid burden in Alzheimer's disease dementia, mild cognitive impairment, and normal aging. *Alzheimers Dement.* Oct 2013;9(5 Suppl):S72-83. PMID 23375563
28. Doraiswamy PM, Sperling RA, Johnson K, et al. Florbetapir F 18 amyloid PET and 36-month cognitive decline: a prospective multicenter study. *Mol Psychiatry.* Sep 2014;19(9):1044-1051. PMID 24614494
29. Schipke CG, Peters O, Heuser I, et al. Impact of beta-amyloid-specific florbetaben PET imaging on confidence in early diagnosis of Alzheimer's disease. *Dement Geriatr Cogn Disord.* 2012;33(6):416-422. PMID 22814208
30. Ong K, Villemagne VL, Bahar-Fuchs A, et al. 18F-florbetaben Abeta imaging in mild cognitive impairment. *Alzheimers Res Ther.* Jan 16 2013;5(1):4. PMID 23324163
31. Ong KT, Villemagne VL, Bahar-Fuchs A, et al. Abeta imaging with 18F-florbetaben in prodromal Alzheimer's disease: a prospective outcome study. *J Neurol Neurosurg Psychiatry.* Apr 2015;86(4):431-436. PMID 24970906
32. Johnson KA, Minoshima S, Bohnen NI, et al. Appropriate use criteria for amyloid PET: a report of the Amyloid Imaging Task Force, the Society of Nuclear Medicine and Molecular Imaging, and the Alzheimer's Association. *J Nucl Med.* Mar 2013;54(3):476-490. PMID 23359661
33. Alzheimer's Association. Alzheimer's Association statement on FDA approval of florbetapir (Amyvid). 2012; http://www.alz.org/documents_custom/amyvid.pdf.
34. Centers for Medicare & Medicaid Services. National Coverage Determination (NCD) for beta amyloid positron tomography in dementia and neurodegenerative disease (220.6.20), effective 09/27/13. <http://www.cms.gov/medicare-coverage-database/details/ncd-details.aspx?NCDId=356&ncdver=1&bc=AAAAgAAAAAAAAA%3d%3d&>.

Policy History

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08/01/2013	Medical Policy Committee review
08/21/2013	Medical Policy Implementation Committee approval. New policy.
08/07/2014	Medical Policy Committee review
08/20/2014	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
08/06/2015	Medical Policy Committee review
08/19/2015	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2016	Coding update
08/04/2016	Medical Policy Committee review
08/17/2016	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2017	Coding update: Removing ICD-9 Diagnosis Codes
10/05/2017	Medical Policy Committee review
10/18/2017	Medical Policy Implementation Committee approval. Coverage eligibility unchanged.
01/01/2018	Coding update
Next Scheduled Review Date:	10/2018

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