Corporate Medical Policy

Beta Amyloid Imaging With Positron Emission Tomography for Alzheimer's Disease

File Name:	beta_amyloid_imaging_with_positron_emission_tomography_for_alzheimers_disease
Origination:	10/2014
Last CAP Review:	5/2020
Next CAP Review:	5/2021
Last Review:	5/2020

Description of Procedure or Service

Three radioactive tracers (florbetapir F18, flutemetamol F18, florbetaben F18) that bind to beta amyloid and can be detected in vivo with positron emission tomography (PET) have been developed. This technology is being evaluated to detect beta amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer disease (AD) and/or other causes of cognitive decline.

Background
The diagnosis of 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 beta amyloid plaques and intraneuronal neurofibrillary tangles in the cerebral cortex. There can be a range of beta amyloid plaques and neurofibrillary tanges on histopathology that support a low, intermediate or high probability of AD.

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 amnestic or nonamnestic, 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 predementia 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 that is being evaluated is amyloid plaque density in the brain detected in vivo by PET. However, Aβ 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 physiological functions by measuring concentrations of positron-emitting chemicals in the body region of interest. Radiopharmaceuticals used for beta amyloid imaging may be generated in a cyclotron or nuclear generator and introduced into the body by

intravenous injection. A number of ^{11}C and ^{18}F-labeled PET radiopharmaceuticals have been investigated for imaging brain beta amyloid.

Regulatory Status
In 2012, FDA approved florbetapir F18 (Amyvid™; Avid Radiopharmaceuticals [a subsidiary of Eli Lilly], Philadelphia, PA) 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 beta amyloid 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 beta-amyloid 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 beta amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer disease and other causes of cognitive decline." Prescribing information for all 3 agents states:

- The objective of beta amyloid image interpretation "is to estimate beta-amyloid neuritic plaque density in brain gray matter, not to make a clinical diagnosis."
- A positive beta amyloid scan "does not establish the diagnosis of AD or other cognitive disorder."
- A negative beta amyloid 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."

Related Policy
Dopamine Transporter Imaging With Single-Photon Emission Computed Tomography

******Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.***

Policy

Beta amyloid imaging with positron emission tomography (PET) is considered investigational for all applications. BCBSNC does not provide coverage for investigational services or procedures.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When Beta amyloid imaging with positron emission tomography (PET) is covered

Not applicable.

When Beta amyloid imaging with positron emission tomography (PET) is not covered

Beta amyloid imaging with positron emission tomography (PET) is considered investigational for all applications.

Policy Guidelines

For individuals who have MCI who receive Aβ imaging with PET, the evidence includes studies on diagnostic accuracy and an RCT that evaluated changes in diagnosis and changes in management. Relevant outcomes are test performance measures, symptoms, and functional outcomes. Studies evaluating the diagnostic accuracy of Aβ PET in patients with MCI, using conversion to probable AD as a reference standard, report that patients with a positive Aβ PET scan at baseline have an increased risk of conversion to probable AD at 3 years. The negative predictive value of Aβ PET in these studies ranged from 77% to 95%. There are currently no disease-modifying drugs, and direct evidence of improved health outcomes with this technology is lacking. An RCT tested immediate vs delayed reporting of Aβ test results for patients with MCI and AD. No differences between the groups were found for health outcomes, although the study was not powered for these outcome measures. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals who have dementia who receive Aβ imaging with PET, the evidence includes studies on diagnostic accuracy and an RCT that evaluated changes in diagnosis and in management. Relevant outcomes are test performance measures, symptoms, and functional outcomes. One possible use of Aβ testing is as an adjunct to clinical diagnosis to rule out AD, which could lead to further diagnostic testing to determine the etiology of dementia and avoidance of unnecessary medications. The pivotal trials showed a sensitivity of 86% to 93% and a specificity of 86% to 100% compared with the criterion standard of Aβ plaque density on postmortem histology. However, the patients in these studies were at the end of life and not representative of the population of patients with suspected AD who present earlier in the course of the disease. Due to the lack of a criterion standard in living patients and limited follow-up, the sensitivity and specificity of Aβ PETin patients with suspected AD areunknown. Direct evidence of improved health outcomes with this technology is lacking. An RCT that tested immediate vs delayed reporting of Aβ test results for patients with MCI and AD found changes in diagnosis and management, but the effect of these changes on health outcomes such as quality of life, symptoms, and functional outcomes is uncertain. The evidence is insufficient to determine the effects of the technology on health outcomes.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: *A9586, A9599, Q9982, Q9983*

The PET scan would be reported using 78811 or 78814.

BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

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 2012; 8(1):1-13. Available online at: http://www.alzheimersanddementia.com/article/S1552-5260(11)02980-3/fulltext . Last accessed October 2014.

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Specialty Matched Consultant Advisory Panel review- 6/2016

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BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.55, 9/14/2017

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.55, 9/13/2018

BCBSA Medical Policy Reference Manual [Electronic Version]. 6.01.55, 9/12/2019

Specialty Matched Consultant Advisory Panel 04/2020

Policy Implementation/Update Information

10/28/14 New policy developed. Beta amyloid imaging with positron emission tomography (PET) is considered investigational for all applications. Medical Director review 10/2014. (sk)

7/28/15 Specialty Matched Consultant Advisory Panel review 6/24/2015. Reference added. No change to policy statement. (lpr)

12/30/15 Added HCPCS codes C9458 and C9459 to Billing/Coding section for effective date 1/1/2016. (lpr)

7/26/16 Codes Q9982, Q9983 added to Billing/Coding section. Specialty Matched Consultant Advisory Panel review 6/29/2016. No change to policy statement. (an)

6/30/17 Updated Policy Guidelines. Added reference. Specialty Matched Consultant Advisory Panel review 5/26/2017. No change to policy statement. (an)

6/29/18 Updated Description and Policy Guidelines sections. Added reference. Codes C9458 and C9459 deleted from Billing/Coding section. Specialty Matched Consultant Advisory Panel review 5/23/2017. No change to policy statement. (an)

6/11/19 Updated Policy Guidelines. Added reference. Specialty Matched Consultant Advisory Panel review 5/15/2019. No change to policy statement. (an)

6/9/20 References updated. Specialty Matched Consultant Advisory Panel review 5/20/2020. No change to policy statement. (eel)