Medical Coverage Policy | β-Amyloid Imaging with Positron Emission Tomography (PET) for Alzheimer's Disease

EFFECTIVE DATE: 04|05|2016
POLICY LAST UPDATED: 03|21|2017

OVERVIEW

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

MEDICAL CRITERIA

Not applicable

PRIOR AUTHORIZATION

Not applicable

POLICY STATEMENT

BlueCHiP for Medicare

Coverage of amyloid PET is covered for BlueCHiP for Medicare members only as part of the Centers for Medicare and Medicaid Services (CMS) approved clinical trial. Refer to Related Policy section.

Commercial Products

Beta amyloid imaging with positron emission tomography is not medically necessary as the evidence is insufficient to determine the effects of the technology on health outcomes.

COVERAGE

Benefits may vary between groups/contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage, or Subscriber Agreement for limitations of coverage when services are not medically necessary or clinical research study benefits/coverage.

BACKGROUND

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 Aβ 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 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 Aβ plaque density in the brain detected in vivo by positron emission tomography (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 physiologic functions by measuring concentrations of positron-emitting chemicals in the body region of interest. Radiopharmaceuticals used for Aβ imaging may be generated in a cyclotron or nuclear generator and introduced into the body by intravenous injection. A number of carbon 11 and fluorine 18 labeled PET radiopharmaceuticals have been investigated for imaging brain Aβ.

Regulatory Status
In 2012, the U.S. Food and Drug Administration (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 Aβ aggregates can be found in cognitively normal elderly patients, as well as patients with AD.

In October 2013 and March 2014, the FDA approved 2 other radioactive diagnostic imaging agents for detecting Aβ 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 Aβ 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 Aβ image interpretation "is to estimate beta-amyloid neuritic plaque density in brain gray matter, not to make a clinical diagnosis."
- A positive Aβ scan "does not establish the diagnosis of AD or other cognitive disorder."
- A negative Aβ 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."

For individuals who have suspected Alzheimer disease (AD) who receive β-amyloid (Aβ) imaging with positron emission tomography (PET), the evidence includes pivotal studies for 3 agents. Literature on the use of Aβ 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 mild cognitive impairment (MCI). The sensitivity and specificity of Aβ 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. Aβ 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 and/or lead to improved outcomes. The evidence is insufficient to determine the effects of the technology on health outcomes. Therefore, this service is not medically necessary for Commercial Products.

CODING

BlueCHiP for Medicare and Commercial Products

The following HCPCS codes **are not medically necessary for Commercial products** and may be allowed for BlueCHiP for Medicare members as part of a CMS-approved clinical study when CMS criteria are met:

A9586 Florbetapir F18, diagnostic, per study dose, up to 10 millicuries
A9599 Radiopharmaceutical, diagnostic, for beta-amyloid positron emission tomography (pet) imaging, per study dose, not otherwise specified (Revised text 1/1/2017)
Q9982 Flutemetamol F18, diagnostic, per study dose, up to 5 millicuries
Q9983 Florbetaben f18, diagnostic, per study dose, up to 8.1 millicuries

Note: If you are treating a BlueCHiP for Medicare member as part of a CMS-approved study, please follow the procedures for correct billing and coding of services found in the policy for Clinical Trials BlueCHiP for Medicare.

RELATED POLICIES

Clinical Trials BlueCHiP for Medicare
BlueCHiP for Medicare National and Local Coverage Determinations
High Tech Radiology Services
Radiopharmaceuticals

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