CMS Manual System	Department of Health & Human Services (DHHS)
Pub 100-03 Medicare National Coverage Determinations	Centers for Medicare & Medicaid Services (CMS)
Transmittal 164	**Date: March 27, 2014**
	Change Request 8526

Transmittal 160, dated February 6, 2014 is being rescinded and replaced by Transmittal 164, dated March 27, 2014 to update the reference to the correct CPM chapter 13 in the first business requirement. All other information remains the same.

SUBJECT: Medicare National Coverage Determination (NCD) for Beta Amyloid Positron Emission Tomography (PET) in Dementia and Neurodegenerative Disease

I. SUMMARY OF CHANGES: The purpose of this Change Request (CR) is that effective for claims with dates of service on or after, September 27, 2013, Medicare will only allow coverage for PET Aβ imaging (one PET Aβ scan per patient) through coverage with evidence development (CED) to: (1) develop better treatments or prevention strategies for AD, or, as a strategy to identify subpopulations at risk for developing AD, or (2) resolve clinically difficult differential diagnoses (e.g., frontotemporal dementia (FTD) versus AD) where the use of PET Aβ imaging appears to improve health outcomes, when the patient is enrolled in an approved clinical study under CED.

EFFECTIVE DATE: September 27, 2013
IMPLEMENTATION DATE: July 7, 2014

Disclaimer for manual changes only: The revision date and transmittal number apply only to red italicized material. Any other material was previously published and remains unchanged. However, if this revision contains a table of contents, you will receive the new/revised information only, and not the entire table of contents.

II. CHANGES IN MANUAL INSTRUCTIONS: (N/A if manual is not updated)
R=REVISED, N=NEW, D=DELETED-*Only One Per Row.*

R/N/D	CHAPTER / SECTION / SUBSECTION / TITLE
R	1/Table of Contents
N	1/220.6.20 /Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease

III. FUNDING:
For Medicare Administrative Contractors (MACs):
The Medicare Administrative Contractor is hereby advised that this constitutes technical direction as defined in your contract. CMS does not construe this as a change to the MAC statement of Work. The contractor is not obliged to incur costs in excess of the amounts allotted in your contract unless and until specifically authorized by the Contracting Officer. If the contractor considers anything provided, as described above, to be outside the current scope of work, the contractor shall withhold performance on the part(s) in question and immediately notify the Contracting Officer, in writing or by e-mail, and request formal directions regarding continued performance requirements.

IV. ATTACHMENTS:

Business Requirements
Manual Instruction

**Unless otherwise specified, the effective date is the date of service.*

Attachment - Business Requirements

Pub. 100-03	Transmittal: 164	Date: March 27, 2014	Change Request: 8526

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SUBJECT: Medicare National Coverage Determination (NCD) for Beta Amyloid Positron Emission Tomography (PET) in Dementia and Neurodegenerative Disease

EFFECTIVE DATE: September 27, 2013
IMPLEMENTATION DATE: July 7, 2014

I. GENERAL INFORMATION

A. Background: CMS does not currently cover Positron Emission Tomography (PET) beta amyloid (also referred to as PET amyloid-beta (Aβ)) imaging, based on a longstanding general non-coverage of PET except where specifically covered nationally. Another radiopharmaceutical used in PET neuroimaging, fluoro-D-glucose F18 (FDG) PET, is nationally covered for either the differential diagnosis of frontotemporal dementia (FTD) versus Alzheimer's disease (AD) under specific requirements; or, its use in a CMS-approved practical clinical trial focused on the utility of FDG PET in the diagnosis or treatment of dementing neurodegenerative diseases.

Lilly USA, LLC, manufacturer of the radiopharmaceutical florbetapir (Amyvid™) that was approved by the Food and Drug Administration (FDA) in April 2012, requested that CMS reconsider its non-coverage decision of PET Aβ imaging. Lilly asked that CMS provide coverage of PET Aβ imaging as a diagnostic test to "estimate amyloid neuritic plaque density in adult patients with documented cognitive impairment who are being evaluated for AD and other causes of cognitive impairment" (quoting the Amyvid™ FDA-approved label). The label states that a negative florbetapir scan "is inconsistent with a neuropathological diagnosis of AD," and "reduces the likelihood that a patient's cognitive impairment is due to AD." However, a positive scan "does not establish a diagnosis of AD or other cognitive disorder." A Medicare Evidence Development and Coverage Advisory Committee (MEDCAC) meeting was convened on the role of PET Aβ imaging in dementia and neurodegenerative disease on January 30, 2013. The MEDCAC highlighted the paucity of evidence on the actual impact of PET Aβ scanning on patients.

B. Policy: After careful consideration, effective for claims with dates of service on or after, September 27, 2013, CMS believes that the evidence is insufficient to conclude that the use of PET Aβ imaging improves health outcomes for Medicare beneficiaries with dementia or neurodegenerative disease. However, there is sufficient evidence that the use of PET Aβ imaging could be promising in certain scenarios. Therefore, Medicare will only allow coverage for PET Aβ imaging (one PET Aβ scan per patient) through coverage with evidence development (CED) to: (1) develop better treatments or prevention strategies for AD, or, as a strategy to identify subpopulations at risk for developing AD, or (2) resolve clinically difficult differential diagnoses (e.g., frontotemporal dementia (FTD) versus AD) where the use of PET Aβ imaging appears to improve health outcomes, when the patient is enrolled in an approved clinical study under CED.

Health outcomes may include: avoidance of unnecessary or potentially harmful treatment or tests; improving, or slowing the decline of, quality of life (to include maintenance of independence) and cognitive and functional status; and survival. Outcomes may be short term (e.g., related to meaningful changes in clinical management) or long term (e.g., related to dementia outcomes).

NOTE: Contractors should refer to the business requirements below as well as general clinical trial billing requirements at Pub. 100-03, chapter 1, section 310, and Pub. 100-04, chapter 32, section 69. See Pub. 100-03, NCD Manual, chapter 1, section 220.6.20, for the coverage Beta Amyloid PET in Neurodegenerative

disease and dementia, and Pub. 100-04, Claims Processing Manual, chapter 13, section 60.12, for claims processing instructions.

II. BUSINESS REQUIREMENTS TABLE

"Shall" denotes a mandatory requirement, and "should" denotes an optional requirement.

Number	Requirement	Responsibility								
		A/B MAC			DME MAC	Shared-System Maintainers				Other
		A	B	HHH		FISS	MCS	VMS	CWF	
8526-03.1	Effective for claims with dates of service on and after September 27, 2013, Medicare will only allow coverage with evidence development (CED) for Positron Emission Tomography (PET) beta amyloid (also referred to as amyloid-beta (Aβ)) imaging (one PET Aβ scan per patient). Please refer to Pub 100-04, Chapter 13, Section 60.12 for detailed claims processing instructions.	X	X			X				IOCE

III. PROVIDER EDUCATION TABLE

Number	Requirement	Responsibility				
		A/B MAC			DME MAC	CEDI
		A	B	HHH		
8526-03.2	MLN Article: A provider education article related to this instruction will be available at http://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/ shortly after the CR is released. You will receive notification of the article release via the established "MLN Matters" listserv. Contractors shall post this article, or a direct link to this article, on their Web sites and include information about it in a listserv message within one week of the availability of the provider education article. In addition, the provider education article shall be included in the contractor's next regularly scheduled bulletin. Contractors are free to supplement MLN Matters articles with localized information that would benefit their provider community in billing and administering the Medicare program correctly.	X	X			

IV. SUPPORTING INFORMATION

Section A: Recommendations and supporting information associated with listed requirements: N/A

"Should" denotes a recommendation.

X-Ref Requirement Number	Recommendations or other supporting information:

Section B: All other recommendations and supporting information: N/A

V. CONTACTS

Pre-Implementation Contact(s): Brijet Burton Coachman, 410-786-7364 or brijet.burtoncoachman@cms.hhs.gov (Coverage), Wanda Belle, 410-786-7491 or wanda.belle@cms.hhs.gov (Coverage) , Chanelle Jones, 410-786-9668 or chanelle.jones@cms.hhs.gov (practitioner claims processing) , Patricia Brocato-Simons, 410-786-0261 or Patricia.Brocato-Simons@cms.hhs.gov (Coverage) , William Ruiz, 410-786-9283 or William.Ruiz@cms.hhs.gov (institutional claims processing)

Post-Implementation Contact(s): Contact your Contracting Officer's Representative (COR) or Contractor Manager, as applicable.

VI. FUNDING

Section A: For Medicare Administrative Contractors (MACs):
The Medicare Administrative Contractor is hereby advised that this constitutes technical direction as defined in your contract. CMS do not construe this as a change to the MAC Statement of Work. The contractor is not obligated to incur costs in excess of the amounts allotted in your contract unless and until specifically authorized by the Contracting Officer. If the contractor considers anything provided, as described above, to be outside the current scope of work, the contractor shall withhold performance on the part(s) in question and immediately notify the Contracting Officer, in writing or by e-mail, and request formal directions regarding continued performance requirements.

Medicare National Coverage Determinations Manual

Chapter 1, Part 4 (Sections 200 – 310.1)

Coverage Determinations

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(Rev.164, 03-27-14)

220.6.20 -Beta Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease

(Rev.164, Issued: 03-27-14, Effective: 09-27-13, Implementation: 07-07-14)

A. The Centers for Medicare & Medicaid Services (CMS) has determined that the evidence is insufficient to conclude that the use of positron emission tomography (PET) beta amyloid (also referred to as amyloid-beta (Aβ)) imaging is reasonable and necessary for the diagnosis or treatment of illness or injury or to improve the functioning of a malformed body member for Medicare beneficiaries with dementia or neurodegenerative disease, and thus PET Aβ imaging is not covered under §1862(a)(1)(A) of the Social Security Act ("the Act").

B. However, there is sufficient evidence that the use of PET Aβ imaging is promising in two scenarios: (1) to exclude Alzheimer's disease (AD) in narrowly defined and clinically difficult differential diagnoses, such as AD versus frontotemporal dementia (FTD); and (2) to enrich clinical trials seeking better treatments or prevention strategies for AD, by allowing for selection of patients on the basis of biological as well as clinical and epidemiological factors.
Therefore, we will cover one PET Aβ scan per patient through coverage with evidence development (CED), under §1862(a)(1)(E) of the Act, in clinical studies that meet the criteria in each of the paragraphs below.

Clinical study objectives must be to (1) develop better treatments or prevention strategies for AD, or, as a strategy to identify subpopulations at risk for developing AD, or (2) resolve clinically difficult differential diagnoses (e.g., frontotemporal dementia (FTD) versus AD) where the use of PET Aβ imaging appears to improve health outcomes. These may include short term outcomes related to changes in management as well as longer term dementia outcomes.

Clinical studies must be approved by CMS, involve subjects from appropriate populations, and be comparative and longitudinal. Where appropriate, studies should be prospective, randomized, and use postmortem diagnosis as the endpoint. Radiopharmaceuticals used in the PET Aβ scans must be FDA approved. Approved studies must address one or more aspects of the following questions. For Medicare beneficiaries with cognitive impairment suspicious for AD, or who may be at risk for developing AD:

1. *Do the results of PET Aβ imaging lead to improved health outcomes? Meaningful health outcomes of interest include: avoidance of futile treatment or tests; improving, or slowing the decline of, quality of life; and survival.*

2. *Are there specific subpopulations, patient characteristics or differential diagnoses that are predictive of improved health outcomes in patients whose management is guided by the PET Aβ imaging?*

3. *Does using PET Aβ imaging in guiding patient management, to enrich clinical trials seeking better treatments or prevention strategies for AD, by selecting patients on the basis of biological as well as clinical and epidemiological factors, lead to improved health outcomes?*

Any clinical study undertaken pursuant to this national coverage determination (NCD) must adhere to the timeframe designated in the approved clinical study protocol. Any approved clinical study must also adhere to the following standards of scientific integrity and relevance to the Medicare population.

a. *The principal purpose of the research study is to test whether a particular intervention potentially improves the participants' health outcomes.*

b. *The research study is well supported by available scientific and medical information or it is intended to clarify or establish the health outcomes of interventions already in common clinical use.*

c. The research study does not unjustifiably duplicate existing studies.

d. The research study design is appropriate to answer the research question being asked in the study.

e. The research study is sponsored by an organization or individual capable of executing the proposed study successfully.

f. The research study is in compliance with all applicable Federal regulations concerning the protection of human subjects found at 45 CFR Part 46. If a study is regulated by the Food and Drug Administration (FDA), it must be in compliance with 21 CFR parts 50 and 56.

g. All aspects of the research study are conducted according to appropriate standards of scientific integrity (see http://www.icmje.org).

h. The research study has a written protocol that clearly addresses, or incorporates by reference, the standards listed here as Medicare requirements.

i. The clinical research study is not designed to exclusively test toxicity or disease pathophysiology in healthy individuals. Trials of all medical technologies measuring therapeutic outcomes as one of the objectives meet this standard only if the disease or condition being studied is life threatening as defined in 21 CFR §312.81(a) and the patient has no other viable treatment options.

j. The clinical research study is registered on the ClinicalTrials.gov website by the principal sponsor/investigator prior to the enrollment of the first study subject.

k. The research study protocol specifies the method and timing of public release of all pre-specified outcomes to be measured including release of outcomes if outcomes are negative or the study is terminated early. The results must be made public within 24 months of the end of data collection. If a report is planned to be published in a peer reviewed journal, then that initial release may be an abstract that meets the requirements of the International Committee of Medical Journal Editors (http://www.icmje.org). However a full report of the outcomes must be made public no later than three (3) years after the end of data collection.

l. The research study protocol must explicitly discuss subpopulations affected by the treatment under investigation, particularly traditionally underrepresented groups in clinical studies, how the inclusion and exclusion criteria effect enrollment of these populations, and a plan for the retention and reporting of said populations on the trial. If the inclusion and exclusion criteria are expected to have a negative effect on the recruitment or retention of underrepresented populations, the protocol must discuss why these criteria are necessary.

m. The research study protocol explicitly discusses how the results are or are not expected to be generalizable to the Medicare population to infer whether Medicare patients may benefit from the intervention. Separate discussions in the protocol may be necessary for populations eligible for Medicare due to age, disability or Medicaid eligibility.

Consistent with §1142 of the Act, the Agency for Healthcare Research and Quality (AHRQ) supports clinical research studies that CMS determines meet the above-listed standards and address the above-listed research questions.

All other uses are noncovered.