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Lilly Supports the Medical Community's Testimony on the Clinical Utility of Beta-Amyloid Imaging Agents, Such as Amyvi™ (Florbetapir F 18 Injection), During CMS Public Hearing

INDIANAPOLIS, Jan. 30, 2013 /PRNewswire/ -- Leading medical experts in the fields of imaging, neurology and dementia came together today to present evidence supporting the clinical utility of beta-amyloid imaging agents, such as Amyvid™ (Florbetap F 18 Injection), during a public hearing held by the Centers for Medicare & Medicaid Services (CMS), known as a Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) meeting.

The CMS panel voted "low to intermediate confidence" in response to whether there is adequate evidence available to determine whether or not positron emission tomography (PET) imaging of brain beta-amyloid changes health outcomes (improved, equivalent or worsened) in patients who display early symptoms or signs of cognitive dysfunction. Additionally, the panel voted "high confidence" that these conclusions are generalizable to the Medicare beneficiary population. The MEDCAC vote may impact future Medicare coverage decisions for beta-amyloid imaging agents.

Amyvid is indicated for PET imaging of the brain to estimate beta-amyloid plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer's Disease and other causes of cognitive decline. Amyvid is an adjunct to other diagnostic evaluations. Amyvid for intravenous use is a radioactive diagnostic agent that is supplied in 10 mL, 30 mL, or 50 mL multidose vials containing 500-1900 MBq/mL Florbetapir F 18.[1]

"The overwhelmingly positive testimony presented by the medical experts around the clinical utility of beta-amyloid imaging agents reinforces that these tools should be a Medicare covered benefit for patients with cognitive impairment being evaluated for Alzheimer's Disease and other causes of cognitive decline," said Wei-Li Shao , senior director, Alzheimer's Business Division, Eli Lilly and Company. "When making a final coverage decision, we encourage the Centers for Medicare & Medicaid Services to heavily consider the real-world medical experience presented today, and the appropriate use criteria recently released by the Society of Nuclear Medicine and Molecular Imaging and the Alzheimer's Association supporting the use of these imaging agents."

The new guidelines state that amyloid imaging could potentially be helpful in the diagnosis of people with cognitive impairment when considered along with other clinical information, and when performed according to standardized protocols by trained staff. The guidelines also indicate that, although published data is extremely limited, amyloid PET is likely to contribute to better patient care under specific circumstances.[2]

The panel voted on two questions, giving a score from one to five – one being low confidence, five being high confidence. The questions focused on whether there is adequate evidence to determine if PET imaging of brain beta-amyloid changes health outcomes in patients who display early symptoms or signs of cognitive dysfunction, and if the evidence can be generalized to the Medicare beneficiary population.

"These diagnostic imaging agents allow physicians to determine – for the first time – whether *living* patients have beta-amyloid plaques in their brain," said Mark Mintun , M.D., chief medical officer, Avid Radiopharmaceuticals, Inc., a wholly owned subsidiary of Lilly. "This information may impact how physicians ultimately treat their patients by helping inform diagnostic decisions. However, patient outcomes are largely due to the physician's ability to make an accurate diagnosis and recommend an appropriate treatment plan."

About Alzheimer's Disease

By 2030, the total number of Americans aged 65 and over with Alzheimer's Disease is expected to reach 7.7 million.[3] In response to this mounting national health threat, the National Alzheimer's Project Act has brought about renewed urgency and focus on developing new and innovative ways to diagnose, support and treat patients suffering from Alzheimer's Disease.[4]

Alzheimer's Disease is one of many possible causes of cognitive impairment, which can make diagnosis challenging. Alzheimer's Disease and other causes of cognitive impairment share many overlapping symptoms, including deficiencies in memory, visuospatial ability, executive function, behavior and language.[5,6] Furthermore, it is estimated that up to one in five patients clinically diagnosed with probable Alzheimer's Disease during life and do not exhibit Alzheimer's Disease pathology upon autopsy.[7,8]

About Amyvid[1]
Amyvid is a radioactive diagnostic agent that is injected into the bloodstream, where it crosses the blood-brain barrier and selectively binds to amyloid plaques. The fluorine 18 (F 18) isotope produces a positron signal, which is detected by a PET scanner. Physicians who read Amyvid PET scans should complete a comprehensive training program available through live events or online at AmyvidTraining.com.

Indications and Usage[1]
Amyvid is indicated for Positron Emission Tomography (PET) imaging of the brain to estimate beta-amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer's Disease (AD) and other causes of cognitive decline.

A negative Amyvid scan indicates sparse to no neuritic plaques and is inconsistent with a neuropathological 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. A positive Amyvid scan indicates moderate to frequent amyloid neuritic plaques; neuropathological examination has shown this amount of amyloid neuritic plaque is present in patients with AD, but may also be present in patients with other types of neurologic conditions as well as older people with normal cognition. Amyvid is an adjunct to other diagnostic evaluations.

Limitations of Use:

A positive Amyvid scan does not establish a diagnosis of AD or other cognitive disorder. Additionally, the safety and effectiveness of Amyvid have not been established for predicting development of dementia or other neurologic condition, or monitoring responses to therapies.

Important Safety Information[1]

WARNINGS AND PRECAUTIONS
Risk for Image Misinterpretation and Other Errors

- Errors may occur in the Amyvid estimation of brain neuritic plaque density during image interpretation
- Image interpretation should be performed independently of the patient's clinical information. The use of clinical information in the interpretation of Amyvid images has not been evaluated and may lead to errors. Other errors may be due to extensive brain atrophy that limits the ability to distinguish gray and white matter on the Amyvid scan as well as motion artifacts that distort the image
- Amyvid scan results are indicative of the brain neuritic amyloid plaque content only at the time of image acquisition and a negative scan result does not preclude the development of brain amyloid in the future

Radiation Risk

- Amyvid, similar to other radiopharmaceuticals, contributes to a patient's overall long-term cumulative radiation exposure. Long-term cumulative radiation exposure is associated with an increased risk of cancer. Ensure safe handling to protect patients and health care workers from unintentional radiation exposure

MOST COMMON ADVERSE REACTIONS

- The most common adverse reactions reported in clinical trials were headache (1.8%), musculoskeletal pain (0.8%), fatigue (0.6%), nausea (0.6%)

For Full Prescribing Information for Amyvid, visit http://pi.lilly.com/us/amyvid-uspi.pdf.

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About Eli Lilly and Company
Lilly, a leading innovation-driven corporation, is developing a growing portfolio of pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers—through medicines and information—for some of the world's most urgent medical needs. Additional information about Lilly is available at www.lilly.com.

This press release contains certain forward-looking statements about Amyvid™ (Florbetapir F 18 Injection), a radioactive diagnostic agent indicated for brain imaging of beta-amyloid plaques in patients with cognitive impairment who are being evaluated for Alzheimer's Disease and other causes of cognitive decline. This release reflects Lilly's current beliefs; however, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and

commercialization. There is no guarantee that future study results and patient experience will be consistent with study findings to date or that Amyvid will prove to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

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[1] Amyvid [package insert]. Indianapolis, IN: Lilly USA, LLC; 2012.

[2] 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. *Alzheimers Dement.* 2013; doi:10.1016/j.jalz.2013.01.002.

[3] Hebert LE, Scherr PA, Bienias JL, et al. Alzheimer disease in the US population: prevalence estimates using the 2000 census. *Arch Neurol*. 2003;60(8):1119–1122.

[4] US Department of Health and Human Services. National plan to address Alzheimer's disease. http://aspe.hhs.gov/daltcp/napa/NatlPlan.pdf. Published May 15, 2012. Accessed January 22, 2013.

[5] Balasa M, Gelpi E, Antonell A, et al; for the Neurological Tissue Bank/University of Barcelona/Hospital Clinic NTB/UB/HC Collaborative Group. Clinical features and *APOE* genotype of pathologically proven early-onset Alzheimer disease. *Neurology*. 2011;76(20):1720–1725.

[6] Thies W, Bleiler L; Alzheimer's Association. Alzheimer's Association report: 2012 Alzheimer's disease facts and figures. *Alzheimers Dement.* 2012;8:131-168.

[7] Lim A, Tsuang D, Kukull W, et al. Clinico-neuropathological correlation of Alzheimer's disease in a community-based case series. *J Am Geriatr Soc*. 1999;47(5):564–569.

[8] Petrovitch H, White LR, Ross GW, et al. Accuracy of clinical criteria for AD in the Honolulu-Asia Aging Study, a population-based study. *Neurology*. 2001;57(2):226–234.

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