World Molecular Imaging Society

August 2, 2013

BY ELECTRONIC DELIVERY

Louis Jacques, M.D.
Coverage and Analysis Group, Director
Centers for Medicare & Medicaid Services
Department of Health and Human Services
2500 Security Boulevard
Baltimore, MD 21244

Re: **Comment on Proposed Decision Memorandum on Beta-Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease (CAG-00431N)**

Dear Dr. Jacques:

The World Molecular Imaging Society (WMIS) appreciates the opportunity to comment on the Proposed Decision Memorandum on Beta-Amyloid Positron Emission Tomography in Dementia and Neurodegenerative Disease (CAG-00431N).

WMIS recognizes that the Proposed Decision proposes an option for providing a limited number of Medicare beneficiaries with beta amyloid PET through coverage with evidence development (CED). However, WMIS is concerned that the Proposed Decision reflects unwarranted skepticism from CMS about both the current state of the evidence for beta amyloid PET and the value of the consensus Appropriate Use Criteria (AUC) developed by the Alzheimer's Association (in partnership with the Society of Nuclear Medicine and Molecular Imaging). WMIS encourages CMS to adopt a more nuanced approach to both of these key issues—coverage and CED—in its Final Decision.

First, WMIS believes that for certain specific indications as reflected in the Appropriate Use Criteria, the clinical evidence for beta amyloid PET is sufficient to warrant coverage as reasonable and necessary. WMIS cautions that a final decision that simply denies coverage for all indications without distinguishing between them would be unwarranted and limit beneficiary access to beta amyloid imaging.

Second, if CMS nevertheless remains convinced that CED is warranted for certain uses of beta amyloid PET, WMIS is concerned that it will be exceptionally difficult for researchers to craft feasible CED studies that could ever meet the Proposed Decision's proposed thresholds, particularly the use of "randomization and postmortem diagnosis as the endpoint." If CMS is intent on requiring CED for the coverage of beta amyloid PET for certain indications, WMIS encourages CMS to provide significantly more flexibility in both the design of and beneficiary eligibility criteria for such studies.

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Background

WMIS is an international scientific educational organization dedicated to the understanding of biology and medicine through multimodal in vivo imaging of cellular and molecular events involved in normal and pathologic processes, and the utilization of quantitative molecular imaging in patient care. At present, WMIS has over 1,000 members. WMIS was formed in 2011, as a result of the merger of two of the premier molecular imaging societies — the Academy of Molecular Imaging and the Society for Molecular-Genetic Imaging. Between 2006 and 2011, AMI was the sponsor of the original National Oncologic PET Registry (NOPR), and post-merger, WMIS continued to sponsor NOPR 2009 and NOPR (NaF-PET).

WMIS has been deeply involved in supporting the CMS effort to make evidence-based coverage decisions on PET imaging, and presented in support of the current beta amyloid PET reconsideration request at the Medicare Evidence Development & Coverage Advisory Committee (MEDCAC) meeting on January 30, 2013.

General Comments

The burdens of Alzheimer's disease are well known. The Alzheimer's Association has reported that health care costs for people with Alzheimer's disease and other types of dementias will reach $200 billion, with the majority of these costs borne by Medicare and Medicaid. An estimated 5.4 million people are living with Alzheimer's disease. Far too many people with Alzheimer's disease are not diagnosed until their symptoms have become severe. Today Alzheimer's disease pathology only can be inferred through the recognition of a characteristic phenotype. By the time dementia is obvious, deficits often are so pervasive that the typical phenotype may be difficult to recognize.

It is precisely this crucial importance of early diagnosis of Alzheimer's disease that makes the opportunities afforded by beta amyloid PET so compelling and important. Significant advances in the use of imaging have made it possible to detect the onset of Alzheimer's disease, track its progression, and monitor the effects of treatment in people with the disease. One such major advance is the FDA-approved beta amyloid PET tracer florbetapir, whose FDA label states that a negative result is "inconsistent with a neuropathological diagnosis of AD at the time of image acquisition" and "reduces the likelihood that a patient's cognitive impairment is caused by AD." Empowered with increased knowledge of brain pathology through tools like beta amyloid PET, clinicians will be more likely to begin and maintain appropriate treatment. CMS currently pays for many diagnostic tests to diagnose or exclude AD. Rapid diagnosis of the absence of amyloid via imaging may lead to more appropriate treatments, thus limiting the expense and risks of inappropriate uses of AD drug therapies.

Coverage Based on Appropriate Use Criteria

In this context, and based on the clinical evidence submitted in support of the use of beta amyloid PET, WMIS encourages CMS to reexamine the benefits of establishing coverage in the final decision pursuant to the Appropriate Use Criteria (AUC) developed by the Alzheimer's Association in partnership with the Society of Nuclear Medicine and Molecular Imaging. We believe that the AUC constitutes a thoughtful approach to provide access while limiting over-utilization, and that the existing clinical evidence for beta amyloid PET when used in accordance with the AUC parameters is more than sufficient to warrant coverage of beta amyloid PET as reasonable and necessary. Any trepidation on the part of CMS as to the sufficiency of the evidence for the use of beta amyloid PET for other indications should not restrict coverage for those indications where the evidence is compelling. Indeed, there is ample precedent for careful indication-based decisions on whether the same service should be covered outright or through CED. In the context of coverage for FDG-PET for Alzheimer's, on which WMIS was deeply involved, CMS established coverage for the differential diagnosis of fronto-temporal dementia (FTD) and Alzheimer's disease under specific requirements, and authorized coverage through CED studies for other indications.

WMIS recognizes that CMS may be concerned that coverage of beta amyloid PET for certain indications would lead to over-utilization of beta amyloid PET. We believe that this concern can be allayed by the adoption of a coverage standard that reflects the AUC, thereby establishing adequate and sufficient safeguards to prevent overuse of this technology, while still ensuring the availability of beta amyloid PET to beneficiaries for whom it is reasonable and necessary. As we stated in our previous comment letter, any such standards adopted by CMS should be rigorous ones. WMIS endorses CMS making explicitly clear in adopting any such criteria that beta amyloid PET scans should not be used for screening of asymptomatic patients or evaluation of those with no documentation of cognitive decline. Moreover, WMIS reiterates its belief that beta amyloid PET should not be considered reasonable and necessary in patients who present with symptoms and clinical profiles that make their diagnosis clear and confident without the scan, in the judgment of the treating physician.

Coverage with Evidence Development for Other Uses

To the extent that CMS nevertheless remains convinced that CED is warranted for certain uses of beta amyloid PET, WMIS and other stakeholders can provide technical assistance in developing registries or other similar approaches to collect evidence that would inform the eventual coverage of beta amyloid PET. WMIS has extensive experience in this context, having worked closely with CMS over many years in developing and sponsoring the various NOPR CED registries.

Precisely because of this experience, however, WMIS is concerned that researchers who wish to develop CED clinical studies of beta amyloid PET will find it exceptionally difficult and challenging to meet the proposed approval thresholds articulated in the Proposed Decision. For example, the Proposed Decision states that such studies must be "comparative, prospective and

longitudinal, and use randomization and postmortem diagnosis as the endpoint where appropriate." Few, if any, clinical studies can accomplish these aims without extraordinary or prohibitive expense, and it is not clear to WMIS whether any entity qualified to develop a beta amyloid PET study would find it feasible to do so under such parameters. In short, if CMS is intent on requiring CED for the coverage of beta amyloid PET for certain indications, WMIS encourages CMS to provide significantly more flexibility in both the design of and beneficiary eligibility criteria for such studies. As an example, if CMS wished to obtain more data on management changes (for instance, data on decisions—based on the results of a beta amyloid PET scan—to avoid administering expensive medications that may not be appropriate), it is possible that such data could be collected under CED.

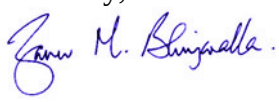
PET Tracers and the CED Trend

Finally, WMIS does want to raise one overall concern regarding the relationship between PET and CED in general. There appears to be a growing trend—starting with FDG-PET, continuing with NaF-PET, and now with beta amyloid PET—of establishing CED as the default coverage status for new FDA-approved PET tracers. PET imaging itself is now a mature and commonplace medical technology, whose value and merit is beyond question in the clinical and scientific community. While each new PET imaging tracer will inevitably come with its own advantages and limitations—as does every drug, device, or technology that comes before CMS for coverage—WMIS advises against requiring every new PET tracer to navigate the lengthy and extensive CED process. We trust that the recent final decision to remove the national non-coverage decision for PET for FDA-approved oncologic applications, combined with the review with beta amyloid for Alzheimer's, will create a foundation for future tracers that enables CMS to avoid proposing CED as a matter of course.

Conclusion

WMIS is committed to working with CMS to ensure that Medicare beneficiaries have access to this important new technology, and to work with physicians and patients to develop guidelines for appropriate use. We look forward to continuing to work collaboratively with CMS, and would be pleased to provide CMS with any additional information that it may find useful in reaching its final decision.

Sincerely,



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President