October 16, 2015

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Centers for Medicare & Medicaid Services
7500 Security Blvd
Baltimore, MD 21244

RE: Comments on Positron Emission Tomography (NaF-18) To Identify Bone Metastasis of Cancer (CAG-00065R) Proposed Decision Memorandum

Dear Director Syrek Jensen:

The Society of Nuclear Medicine and Molecular Imaging (SNMMI), the American College of Nuclear Medicine (ACNM) and the American College of Radiology (ACR) are pleased to provide the following comments on the Proposed Decision Memorandum on Positron Emission Tomography (NaF-18) (CAG-00065R).[1]

SNMMI is an international scientific and professional organization that promotes the science, technology and practical application of nuclear medicine. SNMMI's more than 17,000 members set the standard for nuclear medicine and molecular imaging by creating guidelines, sharing information through journals and meetings, and leading advocacy on key issues.

ACNM is a professional academy composed of physicians and other nuclear medicine professionals dedicated to enhancing the practice of nuclear medicine through the study, education and improvement of clinical practice. The organization is a strong advocate for nuclear medicine professionals and provides access to activities encompassing the business and socioeconomics of nuclear medicine before the legislative and regulatory bodies, other medical organizations, the media and the general public.

ACR is a professional medical society dedicated to serving patients and society by empowering radiology professionals to advance the practice, science and professions of radiological care. The ACR represents over 36,000 members, drawn from radiologists, radiation oncologists, medical physicists, interventional radiologists, and nuclear medicine physicians. For over three quarters of a century, the ACR has devoted its resources to making imaging safe, effective and accessible to those who need it.

SNMMI, ACNM, and ACR appreciate the opportunity to comment on the Proposed Decision Memorandum with regard to Positron Emission Tomography (NaF-18) to identify bone metastasis of Cancer. SNMMI, ACNM, and ACR **disagree strongly with the proposed conclusion, that in this instance, the data available are affirmatively sufficient to determine that NaF PET is <u>not</u> a reasonable and necessary medical service.**

We share the NOPR Working Group position that the published and peer-reviewed research submitted as part of the NOPR reconsideration request, which analyzed NOPR data comprising 35,468 scans

[1] National Coverage Analysis (NCA) for Positron Emission Tomography (NaF-18) to Identify Bone Metastasis of Cancer (CAG-00065R), *available at* http://www.cms.gov/medicare-coverage-database/details/nca-details.aspx?NCAId=233.

performed on 27,713 patients at 1,000 different PET facilities nationwide (data acquired in accordance with the NOPR study design and research protocol approved by CMS), is more than sufficient to demonstrate that NaF PET is reasonable and necessary, and warrants coverage for bone metastasis for all oncologic indications.[2]

In addition to the NOPR data on change of management, a recent study has shown that volumetric tumor burden estimated on a baseline NaF PET/CT is an independent predictor of patient outcomes - overall survival, progression free survival and skeletal related events, after treatment with ^{223}Ra in hormone refractory prostate cancer patients.

I. SNMMI, ACNM, ACR BELIEVE COVERAGE FOR NAF PET IS WARRANTED

A. The Data Submitted are Sufficient for Coverage

Consistent with CMS policy, the NOPR NaF registry undertook prospective data collection of the impact of NaF PET in patients with suspected or known osseous metastasis in any cancer type, using a CMS-approved questionnaire-based approach to assess referring physician–intended management. Structured information on NaF PET scan results was also collected from interpreting physicians.

Additionally, the NOPR Working Group submitted three peer-reviewed manuscripts published in the *Journal of Nuclear Medicine* that summarized the NOPR NaF registry data and results. The first two manuscripts—one on findings in patients with prostate cancer[3] and another on findings in patients with other cancer types (principally breast and lung)[4]—were attached to NOPR's May 2014 letter. The third manuscript, published in February 2015, assessed the impact of NaF PET on treatment monitoring of systemic cancer therapy for bone metastasis.[5] The results reported in these three peer-reviewed publications demonstrated that there remains no clinical need to continue CED data collection for NaF PET for bone metastasis.[6]

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[2] The Proposed Decision states that "the evidence is sufficient to determine that use of a NaF-18 positron emission tomography (PET) scan to identify bone metastasis of cancer is not reasonable and necessary." Given that CMS has proposed to continue CED coverage pending further research, we presume that CMS intended to state that "the evidence is **in**sufficient to determine that use of a NaF-18 positron emission tomography (PET) scan to identify bone metastasis of cancer is ~~**not**~~ reasonable and necessary." To the extent CMS disagrees with our substantive comments and declines to lift the CED restrictions at this time, we would encourage CMS to clarify this phrase throughout its Final Decision.

[3] Hillner BE, Siegel BA, Hanna L, et al. Impact of ^{18}F-fluoride PET in patients with known prostate cancer: initial results from the National Oncologic PET Registry. J Nucl Med 2014;55:1-8. *See also* Segall, GM, PET/CT with sodium ^{18}F-fluoride for management of patients with prostate cancer, J Nucl Med 2014;55:531-533.

[4] Hillner BE, Siegel BA, Hanna L, et al. Impact of ^{18}F-fluoride PET on intended management of patients with cancers other than prostate cancer: results from the National Oncologic PET Registry. J Nucl Med 2014;55:1054-1061.

[5] Hillner BE, Siegel BA, Hanna L, et al. ^{18}F-fluoride PET used for treatment monitoring of systemic cancer therapy: results from the National Oncologic PET Registry. J Nucl Med 2015;56:222-228.

[6] The Proposed Decision repeatedly and inaccurately references these publications as those of "Hillman et al." The lead author of the referenced publications is Dr. Bruce Hillner, the chair of the NOPR Working Group.

As noted in the NOPR reconsideration request, the impact of NaF PET on intended management (classified as either treatment or non-treatment) before and after PET differed substantially between scans done for suspected first osseous metastasis (the most frequent indication) compared to either initial staging or suspected progression of osseous metastasis. In comparing management plans before and after NaF PET in patients receiving systemic therapy for metastatic cancer, four treatment-related options—continue, modify, switch or stop all therapy—were considered. The NaF PET registry also captured detailed categorization of the NaF PET findings from the interpreting physician. These data allowed a broad assessment of whether the differences in post-PET action by cancer types were appropriate in light of the scan findings.

The overall post-NaF PET change in intended management was 40% (42% prostate, 39% breast and 35% all other cancers). After NaF PET, continuing current therapy was planned in 59%, switching therapy in 33%, modifying dose or schedule in 5% and stopping all therapy in 3%. Additionally, the referring physician judged the post-PET prognosis to be better than the pre-PET prognosis in 28% of instances, unchanged in 40% and worse in 32%.

After NaF PET, continuing current therapy was planned in 81% of patients with a better or unchanged prognosis in contrast to those with a worse prognosis where 76% had plans to switch therapy. Among the 57% of patients with prior NaF PET scans for comparison, the plan when the new scan showed either no metastases, a reduction (improvement) in metastatic disease, or no change in metastatic disease was to continue current therapy in 82% of cases. However, when there was worsening or new osseous metastatic disease, the post-NaF PET plan was to switch therapies in 59%.

We strongly believe that the published NOPR data provide evidence of the "changes in management due to test findings" that CMS seeks, and which the CMS-approved study design was intended to collect.[7] The intended management data presented to CMS — and cited by CMS in the Proposed Decision — sufficiently demonstrate that diagnostic information obtained with NaF PET has an impact on physician thinking and formulation of patient management.

Furthermore, while the Proposed Decision indicates that CMS desires additional "confirmatory analyses" to demonstrate that "actual change in management occurred" following NaF PET, SNMMI, ACNM, ACR, in agreement with NOPR, strongly believe that such a confirmatory study is entirely unnecessary. While NaF PET and FDG PET have distinct clinical purposes, the clinicians who perform and utilize NaF PET are by and large the same clinicians who perform and utilize FDG PET. There is no reason to believe that the difference in the diagnostic PET tracer used would have any impact upon the likelihood that the clinician would or would not implement the post-PET intended change in management reported to NOPR.

B. Coverage Should Extend Beyond One Initial Scan

The Proposed Decision suggests that while previous PET decisions (including FDG PET) had differentiated between initial and subsequent treatment, CMS "ha[s] not used this distinction for NaF-18 PET for bone metastasis of cancer since it applies more directly to early diagnostic evaluation than to advanced metastatic disease."[8] We are concerned that if CMS does cover NaF PET, coverage will be limited to one "initial scan" only. Doing so would not be consistent with clinical or with the current Medicare coverage

[7] Proposed Decision at 5.

[8] Proposed Decision at 4.

of FDG PET, which CMS allows to be used for diagnostic evaluation of patients as part of subsequent management decision making (e.g., treatment monitoring, restaging after completion of treatment, detection of suspected recurrence), as well as for diagnosis and initial staging. **We encourage CMS to clarify its position in this regard in its Final Decision.**

C. Coverage Should Include Both Oncologic and Limited Non-Oncologic Indications

In addition to the data published on NaF PET in identifying bone metastasis of cancer, we strongly believe that the evidence indicates that NaF PET is equal or superior to the current covered technology of conventional BS for non-oncologic bone imaging purposes. Section IV of the reconsideration request focuses specifically on these non-oncologic benefits, and expressly requested that CMS "cover NaF PET for bone imaging across a spectrum of non-cancer/benign bone diseases, and favor authorizing *local contractor discretion* for the use of NaF PET across the broad universe of benign indications."[9] We were disappointed to note that in the Proposed Decision, CMS declined to address the coverage of non-oncologic uses of NaF PET at all. We continue to believe that NaF can be beneficial for certain limited non-oncologic indications, particularly those that cannot be imaged well with SPECT or SPECT-CT.

II. FEASIBILITY OF A CONFIRMATORY STUDY

CMS appears to indicate in the Proposed Decision that lifting the CED restrictions on NaF PET would be warranted if an additional study confirmed that the changes in intended patient management found by the NOPR were reflected in evidence of actual changes in patient management.[10] We disagree strongly that confirmatory studies of the NOPR results as to the extent of actual change in management are required under the parameters of the CED study as approved by CMS. We also disagree strongly that the absence of such confirmatory studies precludes CMS from covering NaF PET, in light of the significant quantitative analysis demonstrating significant intended changes in patient management as a result of NaF PET.

We believe that the use of oncologic NaF PET for both initial and subsequent treatment is consistent not only with clinical practice but also with the current Medicare coverage of FDG PET, which CMS allows to be used for diagnostic evaluation of patients as part of subsequent management decision making. **We encourage CMS to clarify its position in this regard in its Final Decision.**

Finally, the proposed twelve month window is an exceptionally compressed time frame in which to accomplish this task proposed and avoid a coverage gap for Medicare beneficiaries. We share the NOPR Working Group belief that eighteen months from the Final Decision would be the minimum amount of time necessary for the researchers to obtain the necessary data, draft the requisite analysis, submit for publication, and complete the reconsideration process. We are concerned that a twelve month time limit could lead to a gap in coverage for Medicare beneficiaries, given the time needed for data analysis, submission for peer review publication, and the public comment periods required as part of the NCD reconsideration process.

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[9] Reconsideration Request, at 11.

[10] Proposed Decision at 17.

III. CONCLUSION

SNMMI, ACNM, and ACR believe that the evidence-based conclusions from the NOPR analysis of the extensive NOPR NaF data set strongly support ending the CED data collection requirements. We strongly disagree with the conclusion of the Proposed Decision that the evidence is insufficient in this regard. We urge CMS to review the evidence in the light of the above comments, and to issue a Final Decision authorizing national coverage of NaF PET for bone metastasis for all oncologic indications.

To the extent CMS declines to revisit its Proposed Decision and a confirmatory study is required, we believe that such study should be of limited scope and retrospective. We believe such a study could be based upon linking CMS claims data and NOPR data to determine the relationship between intended management and actual management. Such a study would require the assistance of CMS in expediting the provision of the necessary claims data, as well as a minimum of eighteen months between the date of the Final Decision and the expiration of CED coverage.

Finally, we urge CMS strongly to reconsider the limited use of NaF PET for non-oncologic indications at the local contractor discretion, based on the position we have articulated above and in the original reconsideration request.

Thank you, again, for allowing us to comment. We believe the NOPR data collection on NaF PET has conclusively demonstrated that NaF PET imaging is reasonable and necessary. In our day to day practice, we know it is necessary and is an invaluable tool in the care and treatment of patients.

Sincerely,

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