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Director, Coverage & Analysis Group
Center for Clinical Standards and Quality
Centers for Medicare & Medicaid Services
Mailstop S3-02-01
7500 Security Blvd
Baltimore, MD 21244

Re: Coverage of NGS tumor panels-CAG-00450N

Dear Ms. Jensen,

The American Cancer Society Cancer Action Network (ACS CAN) appreciates the opportunity to submit comments regarding the national coverage decision (NCD) of Next-Generation Sequencing (NGS) diagnostic tests for cancer. ACS CAN, the nonprofit, nonpartisan advocacy affiliate of the American Cancer Society, supports evidence-based policy and legislative solutions designed to eliminate cancer as a major health problem. As the nation's leading advocate for public policies that are helping to defeat cancer, ACS CAN ensures that cancer patients, survivors, and their families have a voice in public policy matters at all levels of government.

Progress in cancer treatment increasingly involves the use of targeted therapies designed only to work within populations of cancer patients with very specific genetic abnormalities. These targeted therapies often do not work absent the required genetic signature, making the accurate diagnosis of mutations within a tumor absolutely critical. Initially, diagnostic tests probed single genes matched to single drugs, but as the number of targeted therapies increased, the approach of testing a tumor using multiple single gene tests has become burdensome and inefficient. Such an approach is often time consuming and at times may not even be feasible because of limited tumor samples available. The advent of next-generation sequencing (NGS) panel testing has marked an important turning point in cancer diagnosis and treatment, allowing comprehensive tumor genetic data to be collected all at once, providing patients and their providers with information to drive treatment choices.

ACS CAN commends CMS for the positive coverage determination of Foundation One's F1CDx FDA-approved companion diagnostic test. Up to now, coverage for NGS panel tests has been inconsistent, and patients have often been faced with paying for such testing out of their own pockets. We also

support the decision to extend coverage to any FDA-approved NGS cancer panel companion diagnostic rather than a single vendor's test. This approach ensures that any NGS cancer panel test obtaining FDA approval as a companion diagnostic will be automatically covered by CMS, without requiring any additional review which might delay patient access. It is important that a patient can trust the results from their diagnostic test, and FDA approval ensures that a test's clinical validity has been verified by a third party.

The second component of the NCD details categories of diagnostic tests that will be contingently covered with requirements for data collection. This coverage with evidence development (CED) allows FDA-approved tests that lack companion diagnostic designation to be covered, and it allows non-FDA approved tests to be covered as part of a National Cancer Institute (NCI) clinical trial. In both cases the tests must be in the National Institute of Health's (NIH's) genetic testing registry (GTR) and the patients tested must be in a patient registry that is able to track patient outcomes. We are very encouraged that this decision provides a way for patients on NCI trials to benefit from NGS testing, which has been a longstanding challenge.

The CED patient registry requirement ensures that data is being collected that could lead to full FDA approval or unconditional CMS coverage, while still providing coverage during the data collection process. We encourage CMS to be mindful of the cost and burden associated with such registries and tailor registry requirements to ensure that the necessary data will be collected to analyze test performance, while at the same time avoiding any unnecessary requirements that might dissuade test developers from utilizing this coverage pathway.

ACS CAN has concerns regarding the implementation of the non-coverage component of the NCD. While coverage of NGS cancer panels has been fairly sparse, some NGS cancer panel tests appear to currently enjoy some level of coverage as a result of formal local coverage determinations (LCDs) or informal CMS policies. We strongly support the overall movement of the marketplace toward FDA-approved NGS cancer panels, but we are also concerned about continued patient access to NGS cancer panel testing during the transition toward the requirement to be FDA-approved. The proposed non-coverage would begin in 90 days and to the degree that some tests previously being covered, this transition would occur relatively rapidly with little time for individual practices to adjust or NGS panel test developers to create transition plans toward either full FDA approval as a companion diagnostic or establishment of the appropriate patient registries needed to comply with CED requirements. We believe that to the extent an NGS cancer panel test is currently being covered by CMS under current policies, or have an active coverage determination underway, these tests should continue to be covered for a period of time while test developers and oncology practices transition to the new policy. This period should not be seen as an opportunity for tests to newly qualify for coverage under pre-NCD

policies, but rather for tests that have demonstrated a history of coverage pre-NCD or are currently in a coverage determination process to continue to be reimbursed for a finite period.

Lastly, we would like to suggest CMS consider modifications or exceptions to the patient restrictions that are part of the NCD. Under the current proposal a patient is eligible to be tested only once at a late stage of disease, yet genetic mutations in cancer are dynamic. Treatment itself can place selective pressure on a tumor and cause it to evolve, meaning that the genetic makeup of a tumor may differ over time and the genetic makeup of metastases may differ from the primary tumor [1]. Restricting the patient to one single opportunity for testing would not capture these changes, and we recommend CMS consider the allowance of retesting after a medically appropriate interval. Furthermore, while genetic tumor testing is currently indicated in late stage or metastatic cancers, this is simply a reflection of the current science. If NGS tumor panel testing were to become medically appropriate in earlier-stage disease, the proposed non-coverage portion of the NCD would appear to preclude the coverage decision from adapting to recognize such changes in evidence-based care. The non-coverage portion of the NCD, therefore, should be modified such that it does not categorically exclude scientific advances from being translated into updates in coverage.

Next-generation sequencing occurs in cancer in a variety of contexts. Testing may be for a panel of somatic mutations in tumor samples, as is described in this NCD, or it may be in the context of germline mutations, and the technology can even be used for testing single genes. We would like to clarify that our assumption is that this NCD is limited to NGS panel testing in tumor samples, and our comments are in that context. We do not believe it is appropriate to apply the proposed NCD to germline testing, single gene testing, or other diseases. If CMS intends the scope of this NCD to apply more broadly, we recommend clarification and request additional opportunities to comment on such an expanded scope of policy.

In summary, we fully support the coverage of NGS cancer panel tests that have been FDA-approved as a companion diagnostic. We support the coverage of non-FDA approved NGS panels as part of NCI clinical trials, and we appreciate the provisional coverage of FDA-approved, but non-companion diagnostic, tests that will provide important reimbursement while additional data is collected on these tests. We encourage care in developing CED registry requirements to carefully balance assurance that needed data is collected while avoiding any unnecessary requirements. To ensure there is no potential disruption to patient access to NGS panel testing, any coverage for NGS panel tests under current CMS policy should be continued during a transitional period. Lastly, any finalized non-coverage decisions should not preclude patients from benefiting from advancing science that improves validated and medically appropriate genetic cancer testing.

Thank you for the opportunity to provide comments on this important issue for cancer patients. If you have any questions, please do not hesitate to contact myself or Mark Fleury (mark.fleury@cancer.org).

Sincerely,

Christopher W. Hansen
President
American Cancer Society Cancer Action Network

1- Merlo, L. M. F., Pepper, J. W., Reid, B. J., & Maley, C. C. (2006). Cancer as an evolutionary and ecological process. *Nature Reviews Cancer*, *6*(12), 924–935. https://doi.org/10.1038/nrc2013