January 16, 2018

Seema Verma
Administrator
Centers for Medicare & Medicaid Services
Department of Health and Human Services
200 Independence Ave, S.W.
Washington, DC 20201

RE: Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450N)

Dear Administrator Verma:

The American Society of Clinical Oncology (ASCO) is pleased to offer these comments in response to the proposed decision memo regarding a National Coverage Determination (NCD) titled Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer.

ASCO is the national organization representing over 42,000 physicians and other healthcare professionals specializing in cancer treatment, diagnosis, and prevention. ASCO members are also dedicated to conducting research that leads to improved patient outcomes, and we are committed to ensuring that evidence-based practices for prevention, diagnosis, and treatment of cancer are available to all Americans, including Medicare enrollees.

ASCO commends CMS’s clear intent to ensure consistency in the reimbursement and performance of Next Generation Sequencing (NGS) diagnostics used in the care of Medicare beneficiaries with advanced cancers. Sophisticated, biomarker-targeted therapies are being increasingly administered to such patients based on abnormalities identified in NGS tests. ASCO supports holding such high-risk tests to a high regulatory standard in order to ensure that physicians and patients have reliable information for clinical decision-making and to advance our understanding of precision medicine.
ASCO also strongly supports provisions to ensure ongoing coverage with evidence development (CED) of other use cases of NGS tests, including when used in clinical trials and with prospective clinical registries. CED programs serve the dual purpose of enabling patient access to emerging NGS tests while also collecting data on how these tests are used to inform clinical decision-making and their impact on patient outcomes. More broadly, these CED provisions could also serve to further advance the field of cancer research through more explicit annotation of test characteristics and performance that will be essential to accurately characterize emerging connections between biomarker targets, associated therapies, and patient outcomes.

ASCO believes that the NCD could be improved by addressing specific concerns and points of clarification, as outlined below.

**CMS should ensure this NCD does not disrupt the coverage and delivery of cancer care.**

Requirements for CED should be broadened to include NGS tests performed in laboratories that are both CLIA-certified and accredited by the College of American Pathologists (CAP) or other molecular laboratory accreditation organizations with deemed status from CMS.

Existing local coverage determinations (LCDs) for NGS tests should also remain in effect.

The NCD as written currently restricts CED, outside of a clinical trial, to FDA-approved or -cleared NGS tests. While ASCO supports increased oversight of NGS tests directing cancer therapy, a more flexible framework is critical to the clinical research enterprise and to support the rapid development of necessary evidence on the clinical utility of NGS tests. Requirements for CED should be broadened in order for NGS tests to develop the data to justify full coverage as well as FDA clearance. NGS tests used in the clinical research setting are often rapidly improved upon at their respective institutions based on emerging data. To that end, the scope of CED defined under B(2)(a) of the draft decision memo should be expanded to include any NGS tests performed in laboratories that are both CLIA-certified and accredited by organizations with deemed status from CMS. Such additional accreditation is recognized as an improvement over existing CLIA requirements for laboratory testing used in patient care, and ensures that NGS tests used in a clinical setting are of high quality and analytical validity.

Additionally, without a defined timeline for implementation, it is not clear how quickly a sufficient number of NGS tests could be brought into compliance with the NCD, as written. Patients and oncology care specialists already frequently rely on NGS tests performed at their hospital or affiliated lab (institutional or commercial) to identify treatment options and determine eligibility for clinical trials. Oncologists are often able to take advantage of reviewing and analyzing the information directly with expert pathologists who are performing these tests, something of high value given the complexity of their interpretation in many cases. Some of these NGS tests are currently approved for coverage at the LCD level, and would fall outside the scope of the proposed NCD. Rather than issue a national non-coverage determination, ASCO
would urge CMS to allow these LCDs to remain in place to prevent any disruptions in coverage and delivery of cancer care.

**CMS should carefully consider the impact of proposed non-coverage language, including non-coverage of repeat NGS testing.**

Proposed non-coverage of repeat NGS testing is problematic – particularly if the medical and clinical context are not taken into consideration. As written, the NCD language that the “patient has not been previously tested using the same NGS test” is ambiguous and could preclude coverage of medically appropriate re-testing and therefore coverage and access to treatment. ASCO clinical practice guidelines generally counsel clinicians and patients that repeat testing is not required for most patients, but some specific clinical circumstances clearly warrant repeat tests. For example, a previously tested primary tumor sample could differ genetically from a new metastatic lesion. In addition, the genomic features of a tumor may change in response to a therapy, and additional testing may be required to determine a course of therapy after non-curative treatment or recurrence. In many cases repeating the “same” NGS test is preferred so that changes in the tumor genomic profile over time can be more readily identified. If different tests are used it may be more difficult to determine if a newly detected alteration was present previously or not.

The decision to re-test and treat in these scenarios should be based on scientific evidence and clinical judgement, without impediments due to coverage or reimbursement policies. Additional clarification on what constitutes re-testing a patient sample with “the same NGS test” would help avoid such impediments. Whether this would only apply to a single NGS test used repeatedly, or also to similar tests of the same analytes or to updated versions of the original test including additional analytes, is not clear.

Similarly, the concluding non-coverage clause of the NCD for all other NGS testing highlights the need for careful consideration of the issues outlined above. CMS could accomplish its goal of facilitating consistent reimbursement and appropriate use of NGS tests to direct patient care solely through the incentives outlined in the NCD. Inclusion of the non-coverage clause could potentially introduce unnecessary impediments to access to medically necessary testing and treatment.

**CMS should further clarify and refine several requirements related to CED.** Screening NGS tests used to qualify patients for trial participation should be broadly covered. The scope of eligible trials should not be narrowed beyond existing CMS policy for qualifying clinical trials. CED requirements should not substantially restrict access to medically appropriate testing and treatment.
While ASCO appreciates and supports the inclusion of CED for NGS tests used in clinical trials, the requirements for such coverage should be clarified and refined. Section B(2)(b) of the draft decision memo appears to permit inclusion of NGS tests beyond those that are an “FDA cleared or approved in vitro diagnostic,” so long as the other requirements of B(2)(b) are met. However, we would appreciate greater clarity on this point, particularly the intent of the word “within” a qualifying clinical trial. Specifically, ASCO interprets this section to mean that qualifying clinical trials would have coverage of NGS tests that are required to qualify a patient for the clinical trial—whether the test is offered “within” the trial or required by the trial—even if they are not FDA cleared or approved in vitro diagnostics. ASCO supports broad interpretation of the language.

CMS’s intent also appears to broadly cover the use of screening NGS tests to facilitate enrollment onto therapeutic clinical trials. However, coverage of tests used to screen patients for a trial, but who do not ultimately enroll, is not explicitly mentioned. As above, ASCO would urge that all such tests be included for CED, in order to facilitate trial enrollment and remove the potential for unexpected costs for patients. It is also not clear whether the CED requirements would only apply to future trials, or what the expectations are for existing trials whose protocols may not meet the proposed requirements.

ASCO also appreciates CMS’s proposed requirements to ensure the scientific rigor of prospective registries and clinical trials eligible for CED. However, we believe that CED for NGS tests should be inclusive enough to permit broad participation, without abandoning existing standards of scientific rigor. As written, many of the requirements in subsection B(2) of the decision summary could significantly restrict CED eligibility and, by extension, severely constrain our ability to learn about the usefulness of NGS in different clinical circumstances. For example, restricting the scope of CED-eligible trials to only National Clinical Trial Network studies, as in subsection B(2)(b)(i), is overly narrow and would exclude many other high quality, rigorously reviewed clinical trials from participation in CED, including commercially-sponsored trials conducted under IND as well as IND or IND-exempt trials conducted by not-for-profit research institutions and foundations.

Additionally, the list of data collection requirements for CED in subsection B(2), while well-intentioned, presents another significant obstacle to qualification for CED under this NCD. Such requirements will have a negative impact on access to testing and treatment, particularly for oncologists practicing in the community. For example, requirements for collection of objective response rate through use of the Response Evaluation Criteria in Solid Tumors (RECIST) will largely preclude participation outside of academic medical centers or research-focused institutions. RECIST can be a valuable tool within clinical trials, but is overly burdensome in the context of prospective registries that could instead rely on documentation of response by the treating oncologist.
The additional requirements listed in section B(2)(c) are duplicative and unnecessary. As was the case with a 2006 draft decision memo (CAG-00071R2) proposing additional standards for the qualification process for clinical trials under Medicare, we believe current policy remains sufficient to ensure the scientific integrity of clinical research, including CED. The 2007 NCD on clinical trials\(^1\) reflects this consensus view that a broad definition of qualifying study designs should support robust clinical research programs. For these reasons, the 2007 standards for clinical research should be referenced as necessary for the CED portions of the NGS NCD, in place of the current list of requirements in subsection B(2)(c).

**CMS should work with the FDA to better outline the requirements of any NGS test submitted by an entity seeking FDA approval or clearance per the proposed NCD.**

ASCO urges CMS to work with FDA to better outline the requirements of any NGS test submitted by an entity seeking FDA approval or clearance to secure coverage per the proposed NCD. Setting aside applying for a complete pre-market review by FDA, the regulatory pathway for demonstrating equivalence to an FDA-approved NGS diagnostic is not clear, and can require substantial time and resources to fulfil. The relationship between CMS’s requirements for CED; FDA’s existing framework for biomarker validation in NGS tests; and the role of third-party approvers to expedite approval decisions warrants further clarification.

ASCO interprets this NCD as an attempt by CMS to broaden and standardize coverage of NGS somatic genomic testing and ensure that non-covered testing is done in a research context where we can increase our knowledge of this rapidly expanding field. While we generally support this goal, we have significant concerns that the proposed NCD might constrain research on potentially useful tests due to excessively burdensome data collection requirements and thereby limit patient access to all but a few NGS tests that have received FDA clearance. We hope that our comments will inform thoughtful improvements to the draft NCD to ensure medically appropriate access to these tests and associated therapies. Thank you for your willingness to consider our comment on the proposed decision memo. Please contact Sybil Green at Sybil.Green@asco.org with any questions.

Sincerely,

Bruce E. Johnson, MD, FASCO
President, American Society of Clinical Oncology