PERSONALIZED MEDICINE COALITION

May 29, 2019

Tamara Syrek Jensen, J.D.
Director, Coverage & Analysis Group
Centers for Medicare & Medicaid Services
Mailstop S3-02-01
7500 Security Blvd.
Baltimore, MD 21244

Sent electronically

RE: Medicare National Coverage Determination for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450R)

Dear Ms. Syrek Jensen:

The Personalized Medicine Coalition (PMC), a multi-stakeholder group comprising more than 200 individuals and institutions across the health care spectrum, thanks the Centers for Medicare & Medicaid Services (CMS) for reopening its *National Coverage Determination (NCD) for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer*. We appreciate the opportunity to comment on the impact that the current NCD may have on Medicare beneficiary access to NGS-based tests for hereditary cancers and to outline opportunities for further CMS engagement with stakeholders to create a coverage environment that accommodates future applications of NGS technologies in patient care.

Personalized medicine is an evolving field that uses diagnostic tools to identify specific biological markers, often genetic, to help determine which medical treatments and procedures will be best for each patient. By combining this information with an individual's medical history, circumstances, and values, personalized medicine allows doctors and patients to develop targeted prevention and treatment plans.

Personalized medicine is helping to shift the patient and provider experience away from trial-and-error and toward a more streamlined process for making clinical decisions, which will lead to improved patient outcomes, a reduction in unnecessary treatment costs, and better patient and provider satisfaction. PMC's members are leading the way in personalized medicine and recommend that patients who may benefit from this approach undergo appropriate testing and tailored treatment as soon as possible during their clinical experiences.

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NGS technologies have played an essential role in advancing our understanding of altered genetic pathways involved in human cancer. PMC appreciates CMS' recognition that NGS is therefore an important technology for identifying cancer patients who may benefit from a specific treatment path. We share CMS' growing enthusiasm for diagnostic innovation, upon which personalized medicine depends, and we appreciate your interest in putting in place policies that will shape an industry with great potential to make the health system more efficient. The comments that follow reiterate concerns raised by PMC in January of 2018 regarding the scope of the proposed NCD and how the NCD could affect coverage for clinical testing services already employed in patient care and those that will be developed in the future.[i]

Statement of Neutrality

Many of PMC's members will present their own responses to CMS and will actively advocate for those positions. PMC's comments are designed to provide feedback so that the general concept of personalized medicine can advance, and are not intended to impact adversely the ability of individual PMC members, alone or in combination, to pursue separate comments with respect to the NCD on NGS for Medicare beneficiaries with advanced cancer or related issues.

Impact on Coverage of Tests for Germline Mutations

PMC applauded CMS for issuing the NCD in 2018 for somatic-based tests utilizing NGS technology that had been FDA-approved or -cleared for use on patients with late-stage cancers. In our 2018 comments on the proposed decision memo, PMC expressed that we shared concerns raised by the American Medical Association and others in the medical community that the proposed national coverage criteria were too restrictive and ran counter to processes firmly established in medical practice. It came to our attention in early 2019 that the terms of the NCD would apply to both somatic and germline NGS-based testing for patients with cancer, thereby extending the non-coverage provisions in the NCD to NGS-based testing for Medicare beneficiaries with early-stage cancer and those at risk for developing certain hereditary cancers.

Patients benefit from having germline testing for hereditary cancers because it can increase their likelihood of identifying an explanatory gene mutation, inform them of their risk for other types of cancers, present opportunities for disease prevention and risk management, and highlight the need for testing of family members.

Germline testing is often highly valuable to patients and providers because it can lead to improved outcomes. It is recommended by key professional organizations including the American Society for Clinical Oncology, the American College of

Obstetricians and Gynecologists, the Endocrine Society[ii], the National Comprehensive Cancer Network (NCCN)[iii], and the American Society of Breast Surgeons.[iv] These recommendations in leading clinical guidelines are particularly important for informing coverage of NGS-based testing for hereditary cancers like breast, ovarian and colon cancer, which are prevalent among the Medicare population. Since 2006, Medicare has allowed coverage of BRCA testing for patients with a personal history of cancer and germline testing for disease management.

Local Coverage Determinations (LCDs) are based on the clinical usefulness of proven biomarkers independent of test methodologies and the status of their regulatory approval for marketing and labeling. Clinicians rely on research findings to help them assess and understand a given patient's disease and to guide treatment decision-making. Thus, in practice, new clinical oncology data often prompt guideline revisions and spontaneous adoption prior to FDA-indicated approval to allow physicians to provide patients with the best care based on the most up-to-date findings. By 2013, many Medicare Administrative Contractors (MACs) had a BRCA testing coverage policy. All states had LCDs in place by 2017 that provided coverage for germline testing of cancer when supported by clinical guidelines, including NGS-based tests for breast, ovarian and colon cancers.

The transmittal from CMS on November 30, 2018, called for non-coverage of germline tests utilizing NGS if not for beneficiaries with advanced (stage III or IV, recurrent, metastatic, refractory) cancer. Imposing these standards for coverage of germline testing does not align with coverage for this type of testing under existing LCDs and is not in line with the practice of medicine supported by current clinical guidelines. We are concerned that hereditary breast and ovarian cancer testing using NGS will not be available to the nearly two-thirds of people with stage I or stage II cancer, and those who are currently identified as at risk through the use of clinically valid and medically necessary testing services already employed in patient care.

Diagnostic tests performed in clinical laboratories are reviewed using well-accepted processes for determining the analytical and clinical validity of tests and are subject to ongoing review by accreditation bodies and through statute. They are often included in prevention, screening and treatment guidelines for specific conditions. If the scope of coverage is not modified, the NCD will lead to blanket non-coverage for many tests and services moving forward, making it difficult for patients to access care that reflects the most up-to-date science. A representative cross-section of PMC's membership urges CMS to modify the scope of coverage to better reflect established patterns of reimbursement and adoption of diagnostic testing in clinical practice.

We do not believe that CMS should limit the ability of providers to use NGS tests that are recommended in clinical guidelines and create additional barriers to Medicare beneficiaries' access to clinically appropriate NGS-based testing. PMC urges CMS to retain national coverage for germline tests that have been FDA-approved or cleared for advanced cancer patients. If germline testing is used to identify targeted treatment, the terms of the NCD should be applied. However, we believe germline-only mutation testing using NGS technology is outside the scope of the NCD, and that the MACs should therefore retain discretion to cover germline tests using NGS technology.

Ensuring Future of Coverage for Applications of NGS Technology

PMC acknowledges that CMS is reconsidering aspects of the NCD related to germline testing utilizing NGS technology and we hope that the Coalition's recommendations on revising the scope of the NCD are helpful. PMC would also like to highlight additional issues raised in our 2018 comments on the proposed decision memo, which present additional opportunities for engagement with stakeholders.

Liquid biopsies are becoming an increasingly important part of personalized medicine and clinical management of cancer patients, particularly in lung cancer, where solid tissue biopsies are often not possible. Liquid biopsies aid in the initial detection of targetable mutations, assist in the identification of acquired resistance mutations in patients who have relapsed on targeted therapies, and allow for provider monitoring of a patient's response to targeted therapies. The NCD only covers liquid biopsies in limited circumstances, whereas some LCDs give many Medicare patients with non-small cell lung cancer access to liquid biopsy NGS tests. CMS should consider data submitted to the MACs in support of the LCDs on liquid biopsy tests and provide an additional opportunity for clinical laboratories and manufacturers to submit supporting evidence for national coverage.

The NCD currently places a lifetime limit on coverage for the use of the same NGS-based test on a patient. Evidence is building that establishes the value of multiple NGS-based tests throughout the duration of a patient's treatment. An NGS-based panel at the time of diagnosis simultaneously checks for multiple clinically actionable mutations that help guide physicians to targeted therapies. NCCN guidelines recommend multiplex testing such as NGS-based platforms for making treatment decisions. New mutations in many cancers are being discovered rapidly. Limiting access to one test in a patient's lifetime could prevent physicians from identifying the accurate first-line targeted therapy that may save that person's life, and in some cases also impede access to subsequent lines of therapy. Thus, in light of the crucial benefits this testing allows patients and providers, we

urge CMS to reexamine its policy on limiting the number of NGS-based tests covered per patient.

Conclusion

Thank you for reopening the NCD and for considering our comments. PMC welcomes the opportunity to serve as a resource for you in continuing to shape coverage policies that impact beneficiary access to NGS technologies so that they achieve the goal we share with CMS of delivering appropriate, efficient, and accessible health care to patients. If you have any questions about the content of this letter, please contact me at 202-589-1769 or cbens@personalizedmedicinecoalition.org.

Sincerely yours,

Cynthia A. Bens
Senior Vice President, Public Policy

CC: Katherine B. Szarama, Ph.D.
Lead Analyst, Centers for Medicare & Medicaid Services

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[i] Personalized Medicine Coalition. *Comment Letter: Centers for Medicare & Medicaid Services — Proposed Medicare Coverage Decision Memorandum for Next Generation Sequencing for Medicare Beneficiaries with Advanced Cancer*. January 17, 2018. http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PMC_Comments_NGS_NCD.pdf

[ii] AIM Specialty Health. *Clinical Appropriateness Guidelines Genetic Testing for Hereditary Cancer Susceptibility. Effective March 31, 2019.* http://aimspecialtyhealth.com/PDF/Guidelines/2019/Mar31/HereditaryCancerSusceptibility.pdf

[iii] National Comprehensive Cancer Network. *Clinical Practice Guidelines in Oncology*. May 1, 2019 https://www.nccn.org/professionals/physician_gls/default.aspx

[iv] American Society of Breast Surgeons. *Consensus Guideline on Genetic Testing for Hereditary Breast Cancer*. February 10, 2019. https://www.breastsurgeons.org/docs/statements/Consensus-Guideline-on-Genetic-Testing-for-Hereditary-Breast-Cancer.pdf