



November 27, 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: Proposed Decision Memo 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 institutions across the health care spectrum, thanks the Centers for Medicare and Medicaid Services (CMS) for reconsidering the *National Coverage Determination (NCD) for Next Generation Sequencing (NGS) in Advanced Cancer* after hearing concerns that the NCD, as previously written, would have limited beneficiary access to germline testing for certain inherited cancers. PMC appreciates that the newly proposed decision memo expands coverage of tests utilizing NGS technology to Medicare beneficiaries with, or at risk for, inherited breast or ovarian cancer at any stage. This memo is an improvement from CMS' original NCD for NGS-based tests, though we believe it still leaves significant gaps in coverage that we urge you to address in the final policy.

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 treatments of late-stage diseases in favor of more streamlined approaches to disease prevention and treatment, 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.

BOARD OF DIRECTORS

President
Edward Abrahams, Ph.D.

Chair
Stephen L. Eck, M.D., Ph.D.
Immatics Biotechnologies

Vice Chair
Jay G. Wohlgemuth, M.D.
Quest Diagnostics

Treasurer
Peter Maag, Ph.D.
CareDx

Secretary
Kimberly J. Popovits
Genomic Health

Bonnie J. Addario
GO2 Foundation for Lung Cancer

Antoni Andreu, M.D., Ph.D.
EATRIS

Steven D. Averbuch, M.D.
Bristol-Myers Squibb Company (ret.)

Randy Burkholder
PhRMA

William S. Dalton, Ph.D., M.D.
M2Gen

Lori Frank, Ph.D.
Alzheimer's Foundation of America

Brad Gray
NanoString Technologies

Kris Joshi, Ph.D.
Change Healthcare

Anne-Marie Martin
Novartis

Susan McClure
Genome Creative, LLC

Howard McLeod, Pharm.D.
Moffitt Cancer Center

J. Brian Munroe
Bausch Health Companies

Lincoln Nadauld, M.D., Ph.D.
Intermountain Healthcare

Michael Pellini, M.D., M.B.A.
Section 32

Hakan Sakul, Ph.D.
Pfizer, Inc.

Michael S. Sherman, M.D., M.B.A.
Harvard Pilgrim Health Care

Mark P. Stevenson, M.B.A.
Thermo Fisher Scientific

Michael Vasconcelles, M.D.
Flatiron Health

Werner Verbiest
Johnson & Johnson

NGS technologies have played an essential role in advancing our understanding of the altered genetic pathways involved in human cancer. PMC appreciates CMS' recognition that NGS is an important technology for identifying cancer patients who may benefit from a specific treatment path. We share CMS' growing enthusiasm for the 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.

PMC applauded CMS in 2018 when the agency issued its first NCD for somatic-based tests utilizing NGS technology that have been approved or cleared by the Food and Drug Administration (FDA) for use on Medicare beneficiaries with late-stage cancers. In our 2018 comments on the proposed decision memo, PMC indicated that it shared concerns raised by 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.

The comments that follow build on issues raised by PMC in January of 2018ⁱ and May of 2019ⁱⁱ regarding the scope of the proposed NCD and how the NCD could impact coverage for clinical testing services already employed in patient care as well as those that will be developed in the future.

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 proposed NCD on NGS for Medicare beneficiaries with advanced cancer or related issues.

Impact of Proposed Coverage Decision on Usage of NGS-based Tests for Beneficiaries with Early-Stage Breast and Ovarian Cancer

Patients benefit from having germline testing for several hereditary cancers because it increases the likelihood of identifying an explanatory gene mutation that can inform them of their risk for developing other types of cancers. Germline testing may also present opportunities for disease prevention and risk management and highlight the need for testing of family members. NGS-based germline testing can lead to improved outcomes – in part, by informing therapeutic options –for hereditary cancers like breast, ovarian, and colon cancer, all of which are prevalent among the Medicare population. Unfortunately, the proposed policy as drafted appears to deny access to testing of Medicare beneficiaries with ovarian or breast cancer, which if intended, would undermine the spirit of the draft NCD.

The proposed NCD only applies national coverage to FDA-approved or FDA-cleared NGS-based germline tests for patients with ovarian or breast cancer. There are currently no FDA-approved or FDA-cleared NGS-based germline tests for breast and ovarian cancer. This strict criterion would therefore leave Medicare beneficiaries with no covered options, despite National Comprehensive Cancer Network (NCCN) guidelines that recommend testing for some of these individuals.

The requirements would also prevent Medicare Administrative Contractors (MACs) from covering the high-quality laboratory-developed NGS-based germline tests that are available for patients with breast and ovarian cancer. PMC does not believe that CMS intended to deny patients access to these important and potentially lifesaving tests. We therefore recommend that CMS allow MACs to use their discretion to cover NGS-based tests for breast or ovarian cancer patients, including those not reviewed by the FDA, along with all other patients with a cancer diagnosis that meet the additional criteria for testing.

Finally, as a point of clarification, we ask that CMS recognize that the scope of the NCD extends beyond ovarian cancer to include epithelial ovarian, fallopian tube or primary peritoneal cancer. These cancers form in the same type of tissue and are treated the same way and, similarly, are caused by inherited gene mutations. Thus, it is important that CMS recognize these related cancers as within the scope of the NCD.

Impact of Proposed Coverage Decision on Usage of NGS-based Tests in Other Circumstances

An additional concern in the proposed NCD is the limitation on coverage for NGS-based germline tests for patients who have not been previously tested using NGS. This language prohibits coverage for any beneficiary who has had a prior NGS-based test for any reason. This new language as well as the existing similar language in the NCD for somatic testing will limit coverage for medically necessary tests in several circumstances. We believe that the final NCD should remove the prohibition on coverage for beneficiaries who have previously had an NGS-based test and allow certain cancer patients to receive both an NGS-based germline and somatic test when necessary. Additionally, a patient may need subsequent germline testing as new genes and variants are identified or in circumstances where less-invasive testing options are used.

It is not uncommon for patients to receive NGS-based somatic tests to guide cancer therapy. As an example, genetic testing for Lynch Syndrome may require a germline and somatic test in certain patients when such testing has been deemed reasonable and necessary in the context of at least one local coverage determination (LCD). An NGS-based molecular microbiology test may also be required to help diagnose an infection.

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 also being discovered rapidly and technology is evolving. Beneficiaries should therefore not be limited to one NGS-based test if the genes implicated in their condition were not known at the time of a previous test or were outside of the reportable range for a specific test.

A patient may also opt to have a liquid biopsy test to avoid a tissue biopsy. A negative liquid biopsy test result does not always mean that a patient is negative for a biomarker of interest and in some instances NCC guidelines dictate that the patient may require reflex tissue testing. Limiting coverage to one test per beneficiary in this situation may influence a patient's initial choice of less-invasive testing and possibly influence a provider's recommendation to order a follow-up tissue test.

Limiting access to one test in a patient's lifetime could therefore 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. CMS should re-examine its policy on limiting the number of NGS-based tests covered per patient in light of the crucial benefits this testing allows patients and providers at diagnosis, recurrence, and/or progression of cancer.

Ensuring Future of Coverage for Applications of NGS Technology

PMC appreciates that CMS reviewed four studies on liquid biopsies at the request of PMC and other commenters. Liquid biopsies are becoming an increasingly important part of personalized medicine and the clinical management of cancer patients. We understand that the NCD does not limit coverage based on how a sample is obtained for performing a diagnostic laboratory test, and, at this time, coverage for liquid-based multi-gene sequencing panel tests will be left to a MAC's discretion when certain patient criteria are met. CMS should continue to engage with stakeholders to ensure that beneficiaries have consistent access to liquid biopsies, with an emphasis on those tests that 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 provider monitoring of a patient's response to targeted therapies.

Finally, monitoring for minimal residual disease (MRD) is guideline-driven and, by definition, is an assessment that is performed more than once during a patient's management, particularly in hematologic cancers. Local Medicare coverage is provided for use of MRD testing in some hematologic cancers, specific to those MACs participating in the MolDx program, but a wider range of cancers may require MRD assessment in the future. A rational framework for MRD utilizing NGS technology should be considered now to ensure coverage for future uses.

Conclusion

Thank you for releasing the newly proposed 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: Joseph Chin, MD, MS
Deputy Director, Coverage and Analysis Group

Lori Ashby, MA
Director, Division of Policy & Evidence Review

Andrew Ward, PhD
Director, Evidence Development Division

Rosemarie Hakim, PhD
Senior Science Advisor, Evidence Development Division

James Rollins, MD, PhD
Medical Officer

Carl Li, MD, MPH
Medical Officer

Kimberly Long
Lead Analyst

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 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*. May 29, 2019. http://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PMC_CMS_NCD_NGS_Germline_Reconsideration.pdf