COLLEGE of AMERICAN PATHOLOGISTS

November 26, 2019

Tamara Syrek Jensen, J.D.
Director, Coverage and Analysis Group
Centers for Medicare and Medicaid Services
7500 Security Boulevard
Baltimore, MD 21244

RE: Proposed Decision Memo for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450R)

Dear Ms. Jensen,

The College of American Pathologists (CAP) appreciates the opportunity to submit comments on the Proposed Decision Memo for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450R).

As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the CAP serves patients, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide. Members of the CAP are experts in molecular pathology and the CAP works to ensure that Medicare beneficiaries have access to tests that help guide clinical diagnosis and care delivered to Medicare beneficiaries.

We thank the Centers for Medicare & Medicaid Services' (CMS) for recognizing the vital importance of expanding coverage of NGS testing methodologies to earlier stage cancers in patients whose inherited DNA variations may put them at risk for developing breast and ovarian cancer. The CAP supports CMS' proposal to guarantee national coverage for FDA approved/cleared tests and to allow Medicare Administrative Contractors (MACs) discretion to cover other NGS-based tests, regardless of cancer stage. However, we remain concerned about several aspects of the proposed changes that, if implemented, would continue to restrict patient access to early stage germline testing and we urge CMS to make the following outlined changes:

Coverage requirements for breast and ovarian cancers

Under the proposed language, patients with hereditary breast and ovarian cancer may receive national coverage only for FDA approved tests. However, there are currently no FDA approved or cleared germline gene mutation tests for breast or ovarian cancers. Furthermore, CMS proposes to allow MACs discretion to determine coverage of other clinical laboratory tests using NGS-based methods when a patient has a cancer diagnosis *other than* (emphasis added) breast or ovarian cancer." The FDA approval requirement excludes coverage for all available non-FDA approved/cleared tests that use NGS-based methods, regardless of how their performance compared to other non-NGS methods used for similar testing. By this standard, all coverage for germline testing is essentially denied for patients with early stage breast and ovarian cancers. Restricting payment for testing in this way would be a grievous error.

We request that CMS remove "other than breast or ovarian cancer" and allow MACs to determine coverage for ALL types of cancers, including breast and ovarian, when the evidence is sufficient and when tests meet the other coverage criteria outlined in the NCD.

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One test per patient requirement

A. One of the proposed requirements for coverage is that a patient has "not been previously tested using NGS." It is unclear from this statement if this refers to just one method of testing using NGS technology, or if it applies to all testing methods using NGS. For example, the implication is that, if a patient has had a somatic NGS-based test like EGFR and KRAS, it would preclude a germline NGS-based test for BRCA.
We request that CMS replace the proposed coverage criteria that states: "not been previously tested using NGS" with, "not been previously testing using the same NGS-based test for the same primary cancer diagnosis."

B. While repeated testing of an individual's genome for inherited diseases is generally not reasonable and necessary, rapid gains in methodology and gene data base have demonstrated the need for some repeat germline testing for hereditary breast cancer. For example, inherited breast cancer tests used to only examine BRCA1 and 2, but use of a larger cancer panel has increased the diagnostic rate significantly from 2.5% (BRCA1/2 alone) to 6.3% using a guideline panel (11 genes) and 9.4% using a large cancer panel (80 genes) in a cohort of 959 patients (Beitsch et al. 2019).[1]

Further modifications to protocols, techniques and instruments for NGS continue to provide significant improvements in the detection of germline variants associated with inherited cancer today compared to earlier tests. As expanded panel tests become more widely adopted it is imperative that CMS keep pace to reflect quality health care for Medicare beneficiaries.

We request that CMS allow for repeat germline testing when additional implicated genes are included in a test; when the reportable range in genes already tested has been expanded to encompass pathogenic variants for which there is sufficient evidence for clinical testing; or when the analytic sensitivity has improved since the time of the previous test to allow the detection of difficult variants such as mosaic variants, copy number variants or triplet repeat alleles.

Cancer Stage

The Proposed Decision Memo states CMS' intention to cover NGS based technology for germline testing in breast and ovarian regardless of stage, yet the proposed changes to Sections B.2. "Nationally Covered Indications" and Section D "Other", make no reference to cancer stage. Additionally, the NCD title causes further confusion by referring only to Medicare beneficiaries with *advanced cancer*.

To avoid confusion, **we request that the final NCD be modified to reflect coverage for NGS-based germline testing for breast and ovarian cancer regardless of the patient's cancer stage. Additionally, we urge CMS to retitle the NCD to more accurately reflect the new revised policy.**

Thank you again for the opportunity to provide comments on the proposed changes to the NCD. We appreciate CMS' ongoing commitment to ensure that Medicare beneficiaries with cancer have access to clinically indicated testing for both tumor and germline mutations.

Please contact Nonda Wilson, nwilson@cap.org with any questions regarding these comments or if we can provide additional information to CMS on this important national coverage determination.

[1] Beitsch, P.D., et al., Underdiagnosis of Hereditary Breast Cancer: Are Genetic Testing Guidelines a Tool or an Obstacle? J Clin Oncol, 2019. 37(6): p. 453-460.

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