COLLEGE of AMERICAN PATHOLOGISTS

May 29, 2019

Katherine B. Szarama, PhD
Lead Analyst
Coverage and Analysis Group
Centers for Medicare & Medicaid Services
7500 Security Blvd
Baltimore MD 21244

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

Dear Dr. Szarama:

The College of American Pathologists (CAP) appreciates the opportunity to comment on CMS' reconsideration of the national coverage Determination "Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450N) as it relates to the evidence available for tests of germline mutations to identify those with hereditary cancer who may benefit from targeted treatments based on results of the tests. As the world's largest organization of board-certified pathologists and leading provider of laboratory accreditation and proficiency testing programs, the CAP serves patients, patient-facing healthcare providers, pathologists, and the public by fostering and advocating excellence in the practice of pathology and laboratory medicine worldwide.

The CAP supports CMS' reconsideration of germline testing in response to stakeholder concerns that the current NCD excludes germline NGS-based testing from Medicare coverage for patients with early-stage cancers. CMS' decision in March 2019 to include germline testing in its NCD adversely impacts Medicare beneficiaries who are more likely to benefit from the use of treatments designed for earlier stage cancers.

Consensus guidelines and studies support the use of germline testing using NGS-based technology in patients with early stage cancers in some circumstances and the CAP believes that Medicare Administrative Contractors (MACs) should have the discretion to cover these services through the issuance of local coverage determinations (LCDs).

For example, in a multi-center study of over 900 patients, Beitsch and colleagues[1] evaluated the capability of the National Comprehensive Cancer Network guidelines to identify patients with breast cancer with pathogenic variants in expanded panel testing. Patients who have a personal or family history suggestive of a single inherited cancer syndrome are most appropriately managed by genetic testing for that specific syndrome. When more than one gene can explain an inherited cancer syndrome, then multi-gene testing may be more efficient and/or cost-effective. Of the patients tested, over 8% demonstrated a pathologic/likely pathologic (P/LP) variant. The authors' results also showed that by only testing those patients that met current testing guidelines (e.g. NCCN), they missed nearly half of patients with breast cancer with a P/LP variant which could have clinical management implications. The authors proposed that testing criteria be expanded to include all patients with a diagnosis breast cancer.

Further, Kurian and colleagues, who are on the forefront of assessing the prevalence of germline pathogenic variants in breast and ovarian cancer patients, conducted a population-based retrospective cohort study of patients with breast cancer diagnosed from January 2013 to December 2015, accrued from the Surveillance, Epidemiology, and End Results (SEER) registries across Georgia and in California. The study found that Multiple-gene sequencing rapidly replaced BRCA1/2-only testing for patients with breast cancer in the community and enabled two-fold higher detection of

clinically relevant pathogenic variants without an associated increase in prophylactic mastectomy. However, they do note that areas for improvement to further increase the clinical utility of multiple-gene sequencing include postsurgical delay and racial/ethnic disparity in variants of uncertain significance.[2]

Yet another study by Kurian and colleagues on genetic testing among patients with breast and ovarian cancer on women 20 years of age or older in California and Georgia between 2013 and 2014, found that clinically tested patients with breast and ovarian cancer in two large, diverse states had 8% to 15% prevalence of actionable pathogenic variants. The study concluded that substantial testing gaps and disparities among patients with ovarian cancer are targets for improvement.[3]

These and other studies support the CAP's belief that MACs should have discretion to cover germline testing in patients with early stage cancers**.** Prior to the NCD, MACs had developed LCDs that provided coverage for BRCA1 and BRCA2 testing, the treatment of non-small cell lung cancer, acute myelogenous leukemia, and myelodysplastic syndromes using multi-gene panels.[4,5,6,7] These LCDs, which were developed using traditional local coverage development processes, defined reasonable and necessary criteria, were solidly evidence-based policies supported by multiple professional practice guidelines, and were written with substantial input from recognized professionals in multiple institutions. Thus, while the CAP supports the current NCD that allows MACs to determine coverage of NGS laboratory developed tests for patients with advanced cancer, we recommend that MACs be allowed to continue discretionary coverage of NGS-based testing in early stage cancers where testing is found to be reasonable and necessary.

In summary, it is essential that CMS maintain coverage for medically necessary NGS-based tests. **The CAP urges CMS to revise Section D of NCD 90.2 to allow MACs the discretion to make coverage decisions for Medicare beneficiaries with early stage cancers using NGS technology and that hereditary cancer tests previously covered under local Medicare coverage policies be reinstated.**

Thank you for your consideration of our comments. We appreciate CMS' engagement with the CAP and other stakeholders on this issue and we welcome the opportunity to work with the agency to address this important issue that affects the medical care of beneficiaries.

College of American Pathologists

References

1. Beitsch PD, Whitworth PW, Hughes K, et al. Underdiagnosis of Hereditary Breast Cancer: Are Genetic Testing Guidelines a Tool or an Obstacle?. *J Clin Oncol*. 2019;37(6):453-460.

2. Kurian AW, Ward KC, Howlader N, et al. Genetic Testing and Results in a Population-Based Cohort of Breast Cancer Patients and Ovarian Cancer Patients. J Clin Oncol. 2019;37(15):1305-1315.

3. Kurian AW, Ward KC, Hamilton AS, et al. Uptake, Results, and Outcomes of Germline Multiple-Gene Sequencing After Diagnosis of Breast Cancer. *JAMA Oncol*. 2018;4(8):1066-1072.

4. U.S. Department of Health and Human Services, Centers for Medicare and Medicaid Services. MolDX: BRCA1 and BRCA2 Genetic Testing (L36082). Local Coverage Determinations (LCD) Index. Updated August 23, 2018.

5. U.S. Department of Health and Human Services, Centers for Medicare and Medicaid Services. Genomic Sequence Analysis Panels in the Treatment of Non-Small Cell Lung Cancer (L36376). Local Coverage Determinations (LCD) Index. https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=36376&ver=3 Updated February 3, 2016.

6. U.S. Department of Health and Human Services, Centers for Medicare and Medicaid Services. Genomic Sequence Analysis Panels in the Treatment of Acute Myelogenous Leukemia (AML) (DL36926). Local Coverage Determinations (LCD) Index. https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=36376&ver=3 Updated December 8, 2016.

7. U.S. Department of Health and Human Services, Centers for Medicare and Medicaid Services. Genomic Sequence Analysis Panels in the Treatment of Myelodysplastic Syndromes (MDS) (L37078). Local Coverage Determinations (LCD) Index. https://www.cms.gov/medicare-coverage-database/details/lcd-details.aspx?LCDId=37078&ver=4 Updated October 5, 2017.