PERSONALIZED MEDICINE COALITION

November 13, 2021

Greg McKinney, M.D., M.B.A.
Chief Medical Officer
National Government Services
Medical Policy Unit
P.O. Box 7108
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Sent electronically

RE: Proposed Local Coverage Determination (LCD) on Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms (DL37810)

Dear Dr. McKinney:

The Personalized Medicine Coalition (PMC), a multi-stakeholder group comprising more than 220 institutions across the health care spectrum, appreciates the opportunity to comment on the *National Government Services (NGS) Proposed Local Coverage Determination (LCD) on Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms*.[i] Because of its importance in supporting cancer patients' access to personalized medicine, PMC favors the LCD process moving forward. We are concerned, however, that the proposed LCD incorrectly asserts that "the very concept of precision medicine, involving the widespread assumption of clinical utility for wholesale genetic testing, is coming under new scrutiny." PMC does not believe this is supported by existing evidence, including references provided in the draft LCD.

Personalized medicine is an evolving field in which physicians use diagnostic tests to determine which medical treatments will work best for each patient or use medical interventions to alter molecular mechanisms that cause disease. By combining data from diagnostic tests with an individual's medical history, circumstances, and values, health care providers can develop targeted treatment and prevention plans with their patients.

Personalized medicine is helping to shift the patient and provider experiences away from trial-and-error care of late-stage disease in favor of more streamlined strategies for disease prevention and treatment. 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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Based on the potential of personalized medicine to target treatments to those will benefit, we believe this approach holds the greatest potential for improving patient outcomes and reducing overall health care costs without jeopardizing patient access to the health care interventions they need. Accordingly, we urge NGS to demonstrate increased support of personalized medicine as it considers the currently proposed LCD and those impacting personalized medicine in the future.

Statement of Neutrality

Many of PMC's members will present their own responses to the proposed LCD 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 NGS's proposed *LCD on Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms*.

Recognizing the Current Contributions of Personalized Medicine to Cancer Care and Opportunities for Improvement

Over the past decade, scientific and technological advances have vastly expanded the tools and treatments available to physicians for screening, diagnosing, treating, and monitoring patients based on their individual circumstances and molecular characteristics.[ii] PMC's annual *Personalized Medicine Report* recently showed that the number of personalized medicines on the market in the United States has grown from 132 in 2016 to 286 in 2020, the largest four-year increase since the Coalition began tracking this metric in 2008.[iii] More than 90 of these medicines are cancer drugs.

As recognized in the proposed LCD, technological advancements in personalized medicine include genomic sequencing analysis panels, which have demonstrated value in the care of patients with advanced non-small cell lung cancer and metastatic colorectal cancer. Next-generation sequencing (NGS) comprehensive genomic profiling (CGP) provides significant value to the cancer care paradigm by serving a medical need to preserve scarce tissue samples, enabling accurate results when measuring biomarkers that have treatment implications. NGS CGP can identify actionable gene fusions for on-label treatment of some cancers.[iv] Approaches like these are recommended by the National Comprehensive Cancer Network (NCCN).[v]

PMC appreciates NGS continuing to examine how molecular and other drivers of disease can elevate health care in a number of clinical areas, most notably oncology. Providers are increasingly working to integrate personalized medicine diagnostic tools and treatments into their health care work streams to improve the quality of care they can deliver, but their ability to provide access to the right test and the right treatment is dependent in part on a favorable coverage environment. Therefore, PMC is supportive of the LCD process moving forward. In its final LCD, we encourage NGS to provide access to medically necessary NCCN-recommended testing utilizing genomic sequencing analysis panels and CGP for all Medicare beneficiaries with solid organ neoplasms. Furthermore, the proposed LCD excludes other cancer-related uses of NGS, such as germline testing, circulating tumor DNA testing, and in the treatment of hematologic malignancies. This is inconsistent with the Centers for Medicare and

Medicaid Services NCD 90.2[vi] which was supported[vii] by PMC. We request that these tests be considered for inclusion in the final LCD.

PMC notes a concern that the proposed LCD relies heavily on findings from a study conducted in France[viii] to draw conclusions about the clinical utility of molecular profiling in guiding targeted treatment in the United States. It is our understanding that the primary aim of the French study was to define the nature and incidence of genetic mutations in tumor samples and their results in order to define genetic changes that might be targeted for effective therapy. The study determined that the overall impact on response rate or longer survival for patients in France treated with drugs chosen by molecular profiling was small. We believe that failure to provide eligible patients with safer and more effective targeted therapies is often due to multiple clinical implementation barriers. PMC would argue that the referenced study only highlights problems with operationalizing molecular results in the context of the French health care system. The study does not provide evidence to support questions related to the accuracy of molecular results or their clinical utility. We specifically ask that NGS strike language in the proposed LCD based on this study stating that "the very concept of precision medicine, involving the widespread assumption of clinical utility for wholesale genetic testing, is coming under new scrutiny." We ask also that you discontinue the use of the referenced study in this and future LCDs.

Some key barriers to the successful clinical integration of personalized medicine have historically included education, informatics, patient engagement, internal institutional funding, ensuring high-value testing and data collection practices, and inadequate and inconsistent coverage and reimbursement. Recognizing that these and other challenges associated with the evolving field and our health care system have led to a lag in the uniform adoption of personalized medicine, PMC worked to develop and publish a first-of-its-kind quantitative multi-factorial framework to assess the clinical adoption of personalized medicine among a representative sample of 153 health care providers in the United States.[ix] The study demonstrates that, despite considerable heterogeneity in how clinical institutions are adopting personalized medicine, 83 percent of academic health systems, community health systems, and integrated delivery networks studied scored a two or higher on the five-point scale used to examine their integration efforts, with the majority (61 percent) scoring a two or three. The data from this study indicate a broadening adoption of personalized medicine across the United States health system and demonstrate that the vast majority of health care institutions here are taking steps to integrate personalized medicine in clinical settings based on its potential to improve patient care.

The field's leaders have made considerable progress in addressing some of the key barriers to the successful clinical integration of personalized medicine, but many health care delivery institutions have significant work remaining to ensure that patients benefit from its full scope of clinical and economic advantages. We acknowledge that only 22 percent of institutions scored a four or a five on our multi-factorial integration framework. This reminds us of how important it is to have a full understanding of the clinical adoption challenges in the United States and why there is a need for more investment in strategies that can help providers keep pace with rapid scientific and technological advancements.

Conclusion

Thank you for your work on the proposed LCD and for considering our comments. PMC welcomes the opportunity to serve as a resource for you in continuing to shape this coverage policy that will impact patient access to personalized medicine. If you have any questions about the content of this letter, please contact me at 202-499-0986 or cbens@personalizedmedicinecoalition.org.

Sincerely,

Cynthia A. Bens
Senior Vice President, Public Policy

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[i] National Government Services. *Proposed Local Coverage Determination (LCD): Genomic Sequence Analysis Panels in the Treatment of Solid Organ Neoplasms (DL37810).* September 30, 2021. *https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdid=39112&ver=7*.

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[iii] Personalized Medicine Coalition. *Personalized Medicine at FDA: The Scope and Significance of Progress in 2020.* 2021. https://www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_at_FDA_The_Scope_Significance_of_Progress_in_2020.pdf.

[iv] Davies K, et al. "Wake Up and Smell the Fusions: Single Modality Testing Misses Drivers." *Clinical Cancer Research*. 2019. https://clincancerres.aacrjournals.org/content/25/15/4586.

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[v] NCCN. *Biomarkers Compendium*. https://www.nccn.org/compendia-templates/compendia/biomarkers-compendium.

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NCCN Guidelines: *Colon Cancer (Version 2)*. 2021. https://www.nccn.org/professionals/physician_gls/pdf/colon.pdf.

NCCN Guidelines*: Rectal Cancer (Version 1)*. 2018. https://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf.

[vi] Centers for Medicare & Medicaid Services. *NCD 90.2*. 2018. https://www.cms.gov/medicare-coverage-database/view/ncd.aspx?NCDId=372&ncdver=2&SearchType=Advanced&CoverageSelection=Both&NCSelection=NCA%7CCAL%7CNCD%7CMEDCAC%7CTA%7CMCD&ArticleType=SAD%7CEd&PolicyType=Both&s=All&KeyWord=Next+Generation+Sequencing&KeyWordLookUp=Doc&KeyWordSearchType=Exact&kq=true&bc=IAAAADAAAQAA&

[vii] 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/PMCCorporate/file/PMC_Comments_NGS_NCD.pdf

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/PMCCorporate/file/PMC_CMS_NCD_NGS_Germline_Reconsideration.pdf

[viii] Tannok IF. "Molecular Screening to Select Therapy for Advanced Cancer?" *Annals of Oncology*. 2019. https://www.annalsofoncology.org/article/S0923-7534(19)31172-X/fulltext.

[ix] Agarwal A, Pritchard D, et al. "A Quantitative Framework for Measuring Personalized Medicine Integration into US Healthcare Delivery Organizations." *Journal of Precision Medicine*. 2021. https://www.mdpi.com/2075-4426/11/3/196.