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Director, Coverage & Analysis Group
Center for Clinical Standards and Quality
Centers for Medicare & Medicaid Services
Mailstop S3-02-01
7500 Security Blvd
Baltimore, MD 21244

Re: Coverage of NGS tumor panels CAG-00450R

Dear Ms. Jensen:

The American Cancer Society Cancer Action Network (ACS CAN) appreciates the opportunity to comment on the reopened process for a national coverage decision related to coverage of NGS tumor panels. ACS CAN, the nonprofit, nonpartisan advocacy affiliate of the American Cancer Society, supports evidence-based policy and legislative solutions designed to eliminate cancer as a major health problem. ACS CAN empowers advocates across the country to make their voices heard and influence evidence-based public policy change as well as legislative and regulatory solutions that will reduce the cancer burden.

We commend the Centers for Medicare and Medicaid Services (CMS) for recognizing the restrictions that the previous national coverage determination (NCD) language may have placed on the use of next-generation sequencing (NGS) technology in evaluating germline mutations and we support the proposed expansion of coverage to include germline analysis of breast and ovarian cancer patients. We also support allowing Medicare Administrator Contractors (MACs) to cover non-breast and ovarian cancer germline testing when supported by appropriate evidence.

While the proposed changes with respect to germline testing are welcome, we continue to take issue with several aspects of the NCD that have remained unchanged through several comment periods. Specifically, all versions of the NCD have included language that prohibited MACs from making local coverage determinations (LCDs) for NGS technology in anything other than narrowly defined use cases. This approach continues to indicate a mis-understanding of how the specific NGS test use cases addressed in the NCD fit within the overall landscape of potential uses for NGS technology. As with previous versions of the NCD, CMS is proposing to bar coverage of a wide spectrum of possible future uses of NGS technology without first reviewing evidence for those uses. The narrow reconsideration

excluding issues beyond the proposed germline coverage continues to miss an important opportunity to address shortfalls identified in previous comment periods.

Patient restrictions

Two patient restrictions that are part of the NCD continue to be problematic. Specifically, we are concerned with the late-stage requirement and the single testing requirement.

Late stage

The NCD states "*…a report of results of a diagnostic laboratory test using NGS … can contribute to predicting a patient's response to a given drug: good, bad, or none at all*." This is an accurate statement, and importantly its accuracy is not related in any way to the stage of cancer a patient has. As of today, the FDA-approved companion diagnostic claims happen to be in late-stage cancers, but there is no biological or scientific reason that targeted treatments driven by genetic aberrations will not be developed and employed in early-stage cancers. Under the current NCD, such a positive advancement for patients would be barred from coverage, effectively freezing in time the population that can benefit from targeted therapeutic options. Furthermore, the use of the term "stage" is not utilized in the same way in brain cancers or some hematologic malignancies as it is in other solid tumors, so this restriction further adds confusion and is yet another reason to remove reference to staging.

Single testing

Under the current proposal a patient is eligible to be tested only once at a late stage of disease, yet genetic mutations in cancer are dynamic. The proposed NCD seems to assume that new genetic targets would only occur with a new diagnosis; however, the science is clear that treatment itself can place selective pressure on a tumor and cause it to evolve and develop new mutations [1]. This means that the genetic makeup of the same tumor may differ over time and the genetic makeup of metastases may differ from the primary tumor. Clinically this may manifest as the development of resistance to treatment. When such a resistance develops, it may be appropriate to retest in order to identify the new genetic makeup of the same tumor. Restricting the patient to one single opportunity for testing would not capture these changes, and we recommend CMS consider the allowance of retesting after a medically appropriate interval or indication such as acquired resistance.

Lastly, NGS may be used for purposes other than initial diagnosis of a cancer. For example, NGS technology may be used to monitoring the presence or absence of cancer burden within a patient by sampling DNA found in bodily fluids. By its very nature, the monitoring function would require periodic testing.

Technical corrections

A number of technical omissions or errors appear to have been made in Appendix B, which contains proposed decision language.

Following Section B.2., new text (in red) was inserted reading:

"Effective for services performed on or after [Month/XX] [Day/XX], [20XX], the CMS, proposes that NGS as a diagnostic laboratory test [is reasonable and necessary] when performed in a CLIA-certified laboratory, when ordered by a treating physician and when all of the following requirements are met:"

The words "is reasonable and necessary" seem to have been omitted in this text and we recommend inserting them (see bracketed text above).

The next paragraph describes patient characteristics, but the language regarding previous testing is ambiguous:

- "not been previously tested using NGS."

NGS is a technology that could be used in hundreds of contexts, so the assumption is that you do not intend to bar the use of a specific NGS test because a patient has ever been tested for any other disease or condition using a separate unrelated NGS-based test. We propose that you amend this requirement replacing the language referenced above with language in use elsewhere in the existing NCD:

- "not been previously tested using the same NGS test for the same [purpose] "

This same drafting error occurs in the new language proposed under Section D as well and we make the same recommendation as above to clarify.

The non-coverage provision (section C) references patient characteristics under Section B.1., but the newly proposed ovarian and breast allowed uses are not under a numbered section. Is the intention to incorporate these new uses under B.1. and B.2.?

Conclusion

On behalf of ACS CAN we would like to reiterate the ask made in our previous comments [2,3] to request the removal of the noncoverage provisions represented in sections C and D of the NCD, both to preserve existing LCDs as well as to allow coverage policies to adapt to the ever-changing scientific and clinical landscape of genetic testing beyond single companion diagnostic testing of late-stage solid tumors. Research is rapidly driving advances in cancer care, and CMS policies should not deny cancer

patients access to the fruits of that research because of an artificial block on a large swath of use cases of this emerging technology. CMS has recognized this dynamic scientific environment with respect to MAC flexibility to cover new germline use cases, but has continued to block appropriate new coverage cases in the somatic testing space. If you have any questions, please feel free to contact me or have your staff contact Mark Fleury (mark.fleury@cancer.org).

Sincerely,

/Filed electronically/

Lisa A. Lacasse, MBA
President
American Cancer Society Cancer Action Network

1- Merlo, L. M. F., Pepper, J. W., Reid, B. J., & Maley, C. C. (2006). Cancer as an evolutionary and ecological process. Nature Reviews Cancer, 6(12), 924–935. https://doi.org/10.1038/nrc2013

2-American Cancer Society Cancer Action Network comments on NGS NCD (January 17, 2018) https://www.fightcancer.org/sites/default/files/National%20Documents/ACSCAN_Comments_NGSPanelTesting_NCD_Final.pdf

3-American Cancer Society Cancer Action Network comments on NGS NCD (May 29, 2018) https://www.fightcancer.org/sites/default/files/ACSCAN_NCD_NGS_GermlineReopen29MayFinal.pdf