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CLIENT ALERT

Medicare Expands Access to Genetic Diagnostic Tests for Certain Ovarian and Breast Cancers

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On January 27, 2020, the Centers for Medicare & Medicaid Services ("CMS") issued a national coverage determination ("NCD") that authorizes Medicare coverage of next-generation sequencing ("NGS") as a diagnostic laboratory test for ovarian and breast cancers when certain conditions are met.[1] The new NCD expands the scope of the current Medicare NCD for NGS testing of somatic (acquired) and germline (inherited) gene mutations for patients with advanced cancer that was originally adopted by CMS on March 16, 2018 (hereinafter "2018 Advanced Cancer NCD").[2]

What Is NGS Testing?

NGS is a laboratory testing method that enables rapid sequencing of large sections of an individual's genome (e.g., DNA) derived from a patient's specimen (e.g., blood or saliva). The increased efficiency and reduced cost of NGS has made it feasible for laboratories to analyze large regions of DNA and to deliver a substantial amount of patient genetic data to physicians. In the cancer context, NGS is increasingly used to sequence both tumor (somatic) DNA and relevant regions of the patient's own (germline) DNA in order to inform the physician's treatment plan, including the selection of therapeutic agents.[3]

Background: How Is NGS Testing Currently Covered by Medicare?

The 2018 Advanced Cancer NCD authorized Medicare coverage for NGS testing as a diagnostic laboratory test under specified conditions. Coverage is limited to patients with recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer who have not been previously tested using the same NGS test for the same primary diagnosis of cancer

[1] Decision Memo for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450R), *available at* https://www.cms.gov/medicare-coverage-database/details/nca-decision-memo.aspx?NCAId=296&bc=AAAAAAAAABAA&.

[2] Medicare National Coverage Determinations Manual (Pub. 100-03), Chap. 1, Part 2 (Sections 90 – 160.26), Coverage Determinations, § 90.2 (Rev. 215, 04-10-19), *available at* https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/ncd103c1_Part2.pdf.

[3] *See generally* Epstein Becker Green Client Alert, Obstacles in the Path? Medicare's National Coverage Determination on Next-Generation Sequencing Has Significant Implications for Precision Medicine (Mar. 2018), *available at* https://www.ebglaw.com/content/uploads/2018/03/HCLS-Client-Alert-Medicare-NCD-on-NGS1.pdf.

and who have decided to seek further cancer treatment (e.g., therapeutic chemotherapy). In addition, the NGS test must have received U.S. Food and Drug Administration ("FDA") approval or clearance as a companion in vitro diagnostic ("IVD") with an indication for use in the patient's cancer. Finally, testing must be performed in a CLIA-certified laboratory, and test results must be provided to the treating physician for management of the patient using a report template to specify treatment options.[4]

The 2018 Advanced Cancer NCD also allowed for Medicare Area Contractor ("MAC") discretion for coverage of NGS tests that are not FDA-approved or cleared companion IVDs, when the test is performed in a CLIA-certified laboratory and meets the other criteria set forth in the 2018 Advanced Cancer NCD or the new NCD.[5] However, the 2018 Advanced Cancer NCD did not provide any criteria that the MACs should use to make a coverage decision for an individual NGS test. Nevertheless, the MACs have the option to cover NGS tests on a case-by-case basis or to issue their own local coverage determinations ("LCDs"), which could range from fully positive to fully negative coverage for additional NGS tests.

What Changes Are Being Made in the New NCD?

The new NCD expands the current Medicare coverage for NGS to beneficiaries with breast and ovarian cancers. Coverage will be available for NGS testing if all of the following criteria are met:

- There are clinical indications for germline (inherited) testing for hereditary breast or ovarian cancer;
- The patient has documented risk factors for germline (inherited) breast or ovarian cancer; and
- The patient has not been tested previously with the same germline test using NGS for the same germline content.

In addition, the NGS test must meet the following conditions:

- The FDA must have approved or cleared the test, and
- The laboratory performing the test must provide test results to the patient's treating physician using a report template that specifies available treatment options to assure that the test results are used for managing the patient's treatment.

Although the new NCD focuses on NGS coverage for breast and ovarian cancers, CMS retained the provision in the 2018 Advanced Cancer NCD that allows MACs to authorize coverage for other NGS tests that are not FDA approved or cleared and that are used for patients with a cancer diagnosis other than breast or ovarian cancer, or for non-cancer illnesses, such as heart disease or infectious diseases.

[4] See fn. 2, *supra.*
[5] *Id.*

Does the New NCD Address All NGS Testing Issues?

There are a number of issues left open by the new NCD. One of the most significant issues for innovators is the requirement that a NGS test be approved or cleared by the FDA. Several stakeholders expressed concern that this would adversely affect access to NGS testing, since most laboratories offer NGS as a laboratory developed test ("LDT") that does not require FDA approval. CMS responded to these concerns by noting that an LDT, even if performed by a CLIA-certified laboratory, might not have sufficient evidence to demonstrate its clinical utility; in CMS's view, tests that are FDA approved or cleared are able to demonstrate analytic and clinical validity.

In addition, some stakeholders argued that the additional requirement for an indication-specific FDA approval (for patients with recurrent, relapsed, metastatic, or advanced stage III or IV cancer) suggested that NGS data cannot usefully inform clinical decision making in the absence of a specific FDA-approved therapy tied to testing. Although CMS left open the local MAC coverage pathway, which requires either (1) having to pursue indication-specific FDA approval to qualify under the 2018 Advanced Cancer NCD, or (2) having to seek a coverage determination that is left entirely to the discretion of the MACs, these options can be a significant barrier that could delay or deter the development of new NGS tests.[6]

One encouraging development in the new NCD is that, unlike the 2018 Advanced Cancer NCD, Medicare coverage for breast and ovarian cancers will not be limited to the later stages of the disease; all stages will be covered. Further, FDA approval does not have to be for, or have a cleared indication for, use in that patient's cancer.

The expanded NCD manual language clarifies when NGS is covered for somatic, or acquired, cancers and when NGS is covered for germline, or inherited, cancers. Specifically, NGS is covered for patients with somatic cancers that are either recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancers. In addition, NGS is covered for patients with hereditary breast or ovarian cancers. Nevertheless, given the rapidly developing and accumulating evidence related to the possible uses of NGS testing in various types of cancers and non-cancer illnesses, the new NCD continues to provide considerable discretion to the MACs to make coverage determinations for the use of NGS testing in situations not specifically addressed in the expanded NCD manual language. For example, CMS noted that it was not addressing diagnostic tests for hematologic cancers because its current thinking is that it is unclear if this category of cancers is inherited or acquired. However, CMS acknowledged that "this NCD reconsideration permits coverage decisions regarding coverage of NGS for hematologic malignancies to be made by the MACs."[7]

How Might CMS's Conclusions Impact Coverage for Other Precision Diagnostic Tests?

CMS's expansion of coverage for NGS testing acknowledges the clinical evidence supporting the use of NGS as a diagnostic tool for breast and ovarian cancer to "identify the germline mutations most likely to be targeted by a treatment regimen tailored to certain germline

[6] *See* Javitt, G. H. and Wanerman, R. E., Health Affairs Blog, CMS Coverage Decision May Raise Barriers to Precision Cancer Medicine and Reduce Incentives for Evidence Development (Mar. 22, 2018), *available at* https://www.healthaffairs.org/do/10.1377/hblog20180322.833957/full/.

[7] See fn. 1, *supra*.

mutation" and thereby improve health outcomes of Medicare beneficiaries. According to CMS, the use of NGS in this context "has utility for patients in the discovery of new targeted therapies for inherited cancers and in the physician management of inherited cancers of the breast and ovary in Medicare beneficiaries."[8]

As noted previously, the requirement for FDA approval (and for advanced somatic cancers, an indication-specific FDA approval) sets a high bar that could deter the development of new LDT-based NGS tests. Although the new NCD expresses a preference for using the FDA review process as the preferred pathway for validating a NGS test, it is unclear what evidence a MAC may want to see to approve Medicare coverage for new applications of NGS testing over time.

Further, one area that CMS did not address in the new NCD is coverage for artificial intelligence ("AI") applications as a component of or adjunct to NGS testing. This is an emerging area, and it is unclear if and how CMS will recognize the additional costs and potential benefits from AI as a diagnostic and treatment tool for cancers and other illnesses.

Interested stakeholders should continue to monitor CMS developments related to NGS testing.

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[8] *Id.*