ASSOCIATION FOR MOLECULAR PATHOLOGY

Providing global expertise in molecular testing that drives patient care

6120 Executive Boulevard, Suite 700, Rockville, Maryland, 20852

October 11, 2025

Contractor Medical Director (s) Noridian Healthcare Solutions, LLC
Attention: Draft LCD Comments
4510 13th Ave. S, STE1
Fargo, ND 58103-6646

Submitted electronically via policydraft@noridian.com

Subject: MolDX: Non-Next Generation Sequencing Targeted Molecular Panel Tests for Predictive Testing in Cancer (DL40222)

Dear Medical Directors:

On behalf of the Association for Molecular Pathology (AMP), thank you for the opportunity to comment on the draft Local Coverage Determination (dLCD) entitled MolDX: Non-Next Generation Sequencing Targeted Molecular Panel Tests for Predictive Testing in Cancer.

AMP is an international medical and professional association representing approximately 3,100 physicians, doctoral scientists, and medical laboratory scientists (technologists) who perform or are involved with laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. Membership includes professionals from academic medicine, hospital-based and private clinical laboratories, the government, and the in-vitro diagnostics industry. AMP members are highly involved in the development, validation, and interpretation of molecular diagnostic tests, including targeted molecular panel tests for predictive testing in cancer patients.

AMP greatly appreciates that Noridian proposed favorable coverage of non-next-generation sequencing (NGS) based targeted molecular panel tests for predictive testing in cancer. Tests of this kind, including those that evaluate a single, actionable biomarker, are often instrumental for rapid decision-making purposes when time is of the essence, as is the case for many patients with cancer.

AMP members with expertise in this type of testing have identified several changes outlined in the information below that will help streamline the policy and ensure practitioners are able to order and provide this essential testing to patients.

Coverage Indications, Limitations, and/or Medical Necessity

Removal of NGS Requirement in National Guidelines

AMP is concerned that the current wording in Criterion 2b conflicts with the phrasing used in national consensus guidelines. There is currently no specification stating NGS must (or must not) be used as the initial testing methodology. Most oncology guidelines **recommend** the use of next generation sequencing (NGS), but do **not explicitly require** it.[1]

Additionally, the following sentence in 2b is unclear and vague "*testing by a non-NGS method will provide a rapid result that allows for the prompt and timely management of the* patient".
As there is no definition of rapid result within the coverage policy nor is there a general definition understood by practitioners.

As such, AMP requests that the following definitions be clarified:

- "required by national consensus guidelines"
- "rapid result"

This will allow providers to have a better understanding of the limitations in this coverage policy. If no such definitions exist, AMP strongly recommends deleting **Criterion 2b**, as the current language introduces unnecessary ambiguity that could lead to confusion among providers and potential gaps in patient care.

<u>AMP Seeks Clarification on the Standard Ordering Practices of Providers</u>

When ordering genetic tests, the standard practice, in many cases, requires health practitioners to order both a non-NGS test and an NGS panel concurrently, recognizing each method offers a distinct and complementary purpose. As such, Criterion 3 does not align with standard practice. For example, when rapid treatment decisions are needed based on actionable biomarkers, providers may order targeted single-gene tests to guide treatment decisions while simultaneously ordering NGS panels to capture broader genomic information. The time saved in the NGS process is invaluable when determining cancer prognosis, diagnosis, and treatment options.[2][3]

As such, AMP recommends that the red text with the strikethrough is deleted from criterion 3:

"The patient has not been previously tested by a molecular <u>panel</u> test for the same cancer indication for the same genetic content. ~~NOTE: A negative result (no clinically actionable mutations found) by the non-NGS test may be followed by an NGS test that includes additional necessary non-duplicative genes and genomic positions."~~
This deletion would allow concurrent ordering of non-NGS tests for actionable biomarkers and NGS panels for comprehensive profiling, without creating unnecessary administrative or coverage barriers.

<u>Standard for "Comparable" Accuracy is Undefined</u>

AMP is also concerned with Criterion 6, which requires the accuracy of non-NGS testing to be "comparable" to that of NGS methods. Next generation sequencing is a newer technology that is increasing in accuracy every year as it advances. It is impossible to continually have two methods be "comparable" as the technologies deviate. Therefore, **AMP recommends that this criterion be**

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[1] https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf

[2] https://ascopubs.org/doi/10.1200/JCO.21.02767

[3] https://ascopubs.org/doi/10.1200/PO.22.00715

removed as any further definition has a high likelihood of becoming out of date as technology advances.

Remove Redundant Criteria

AMP recommends removing Criterion 8, as the content is duplicative of the requirements already outlined in the Technical Assessment process. The focus of the coverage criteria should be on outlining coverage and medical necessity for testing, not repeating standards addressed within the technical assessment.

Additionally, if Noridian chooses to maintain Criterion 8, we strongly urge you to revise the following sentence:

"Clinical validity (CV) of any analytes or profiles must be established through a study published in the peer-reviewed literature for the intended use of the test in the intended population with demonstrated reproducibility across clinical study cohorts."

The current language could be misinterpreted to mean that each laboratory must independently publish clinical studies for tests already supported by published evidence. We recommend clarifying that laboratories are not required to generate or publish their own CV data if such evidence already exists in the literature.

If Criterion 8 remains in the final LCD, we urge consistent language across all LCDs, ensuring that these criteria do not impose requirements more stringent than those found in existing technical assessment forms.

Thank you again for the opportunity to review and comment on this draft policy. We are happy to provide additional clinical or other information to assist you as you work towards finalizing the LCD. Please direct your correspondence to Annie Scrimenti, Director of Public Policy and Advocacy, at ascrimenti@amp.org.

Sincerely,
Jane S. Gibson, PhD
President, Association for Molecular Pathology