July 3, 2021

CGS Administrators
Meredith Loveless,
Attn: Medical Review
26 Century Blvd., Ste ST610
Nashville, TN 37214-3685

Noridian Healthcare Solutions, LLC
Part B Contractor Medical Director(s)
Attention: Draft LCD Comments
PO Box 6781
Fargo, ND 58108-6781

Palmetto GBA
Part B Policy
PO Box 100238 (JM) and
PO Box 100305 (JJ)
AG-275 Columbia, SC 29202

Wisconsin Physicians Service
Ella Noel, D.O., FACOI
1717 West Broadway
Madison, WI 53713

Re: MolDX: Next-Generation Sequencing Lab-Developed Tests for Inherited Cancer Syndromes:
CGS Administrators DL39017
Noridian (JE) DL38972 and (JF) DL38974
Palmetto (JJ) and (JM) DL38966
Wisconsin Physicians Service (J5) and (J8) DL39040

Dear Medical Directors,

The Association for Molecular Pathology (AMP) and the College of American Pathologists (CAP) write to provide joint comments on MolDX's proposed coverage policy for Next-Generation Sequencing Lab-Developed Tests for Inherited Cancer Syndromes. We appreciate the opportunity to review and provide joint comments as our organizations share the same perspective regarding this draft LCD.

The Association for Molecular Pathology (AMP) is an international medical and professional association representing approximately 2,300 physicians, doctoral scientists, and medical technologists who perform, or are involved with, laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. Membership includes professionals from the government, academic medicine, private and hospital-based clinical laboratories, and the in vitro diagnostics industry.

The College of American Pathologists (CAP) is the world's largest organization of board-certified pathologists and the leading provider of laboratory accreditation and proficiency testing programs. The CAP serves patients, pathologists, and the public by fostering and advocating for excellence in the practice of pathology and laboratory medicine worldwide.

Together, we would like to thank you for proposing next generation sequencing (NGS) coverage for lab developed tests for inherited cancers. We believe thoughtful consideration was given to this issue and the resulting proposed LCD will positively impact patient care. Further, we appreciate your consideration of the following comments:

I. Coverage Indications, Limitations, and/or Medical Necessity

Comment: This proposed LCD appears to contain language that conflicts with current MolDX LCDs for BRCA1 and BRCA2 Genetic Testing L36082[1] (Billing and Coding Article A56854[2]); Genetic testing for Lynch Syndrome L35024[3] (Billing and Coding Article A54987[4]), and Repeat Germline Testing L38274[5]

(Billing and Coding Article A58017[6]). These policies contain language which includes coverage guidance and next generation sequencing CPT codes that we believe could potentially result in confusion among providers as to which LCD is appropriate to use when ordering and billing NGS panel tests for inherited cancers

Recommendation: We recommend that the MolDX MACs instruct the provider community as to the correct LCD to use when performing NGS panel testing for inherited cancer.

II. Recommendations Regarding Situations in which a Test Should Not Be Used or Coverage is Denied

The third bullet point states that a test is non-covered if:

"It is used to identify a known familial variant(s) that could be identified with a more specific test"

Comment: The phrase "a more specific test" is ambiguous and could be interpreted to mean either a less comprehensive test (one that yields a broader range of nevertheless specific results) or a more focused or targeted test (one the yields a narrower range or a single result); in either case, it does not appear the word "specific" is used in a way that is consistent with its meaning in diagnostic settings. To ensure provider compliance with this Medicare coverage policy and to help avoid inappropriate billing, the phrase "more specific test" should be replaced by terminology which accurately reflects what it appears most likely from context is intended, that is a more narrowly focused or targeted test, which nevertheless addresses the range of clinically relevant potential findings. We ask that this language be revised so that both ordering clinicians and performing laboratorians clearly understand its intent and appropriate application.

Recommendation: We request that the final LCD replace the phrase "a more specific test" with, "a test that is more narrowly focused or targeted, while still addressing the range of clinically relevant potential findings."

III. Criteria for Coverage

The policy provides the following coverage criteria:

- "The test has satisfactorily completed a Technical Assessment (TA) by MolDX for the stated indications of the test."

- "The assay performed includes at least the minimum genetic content (genes or genetic variants) required for clinical decision making for its intended use that can be reasonably detected by the test."

Comment: The AMP and CAP applaud MolDX's efforts to streamline its MolDX Technical Assessment Submission Checklist and Questionnaire M00151, V5. However, the document still appears to be overly burdensome for test applicants. We understand that a test must successfully undergo a TA by MolDx in order to be eligible for coverage, but the TA requires granular submission for test coverage and we believe that the assessment process should provide a corresponding granular rationale for the information that is being requested, so that each question contains a clear and logical expression of its relevance to coverage decisions. This will go a long way to ensuring that the process effectively and efficiently achieves its intended result of ensuring the program beneficiaries are provided timely access to appropriate testing modalities.

Recommendation: We recommend that the MolDX program provide a granular rationale for the information it requests on the TA questionnaire. Specifically, we recommend that the technical assessment document define:

- the rationale for requesting a "yes" or "no" response to questions #1 and #2 in the MolDX Technical Assessment Checklist/Questionnaire M00151, V5, as there is often a "middle ground" as to whether clinical utility/clinical validity has been established in the literature.

Additionally, the requirement that an assay perform at least the minimum genes or gene variants listed on MolDX's Analytical Validity, Clinical Validation Summary Worksheet M00155 v2, is likely to be a moving target since evidence for genes or types of gene variants causing inherited cancer that are not readily detectable by NGS (e.g., structural rearrangement, deep intronic variants not previously targeted) is an evolving area and new guidelines are likely to be forthcoming. It is also possible that a laboratory may need to supplement an NGS assay with a single gene assay or other ancillary assay. When and if this occurs, we encourage MolDx to work with providers to ensure that an update to the required list does not result in non-coverage and reduced patient access to these procedures.

CPT Coding
We recommend the inclusion of additional CPT codes for targeted genomic sequencing. The additional codes include, but may not be limited to, those listed below:

81162	BRCA1 (BRCA1, DNA REPAIR ASSOCIATED), BRCA2 (BRCA2, DNA REPAIR ASSOCIATED) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; FULL SEQUENCE ANALYSIS AND FULL DUPLICATION/DELETION ANALYSIS (IE, DETECTION OF LARGE GENE REARRANGEMENTS)
81163	BRCA1 (BRCA1, DNA REPAIR ASSOCIATED), BRCA2 (BRCA2, DNA REPAIR ASSOCIATED) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
81164	BRCA1 (BRCA1, DNA REPAIR ASSOCIATED), BRCA2 (BRCA2, DNA REPAIR ASSOCIATED) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; FULL DUPLICATION/DELETION ANALYSIS (IE, DETECTION OF LARGE GENE REARRANGEMENTS)
81165	BRCA1 (BRCA1, DNA REPAIR ASSOCIATED) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
81166	BRCA1 (BRCA1, DNA REPAIR ASSOCIATED) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; FULL DUPLICATION/DELETION ANALYSIS (IE, DETECTION OF LARGE GENE REARRANGEMENTS)
81167	BRCA2 (BRCA2, DNA REPAIR ASSOCIATED) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; FULL DUPLICATION/DELETION ANALYSIS (IE, DETECTION OF LARGE GENE REARRANGEMENTS)
81201	APC (ADENOMATOUS POLYPOSIS COLI) (EG, FAMILIAL ADENOMATOSIS POLYPOSIS [FAP], ATTENUATED FAP) GENE ANALYSIS; FULL GENE SEQUENCE
81202	APC (ADENOMATOUS POLYPOSIS COLI) (EG, FAMILIAL ADENOMATOSIS POLYPOSIS [FAP], ATTENUATED FAP) GENE ANALYSIS; KNOWN FAMILIAL VARIANTS
81203	APC (ADENOMATOUS POLYPOSIS COLI) (EG, FAMILIAL ADENOMATOSIS POLYPOSIS [FAP], ATTENUATED FAP) GENE ANALYSIS; DUPLICATION/DELETION VARIANTS
81212	BRCA1 (BRCA1, DNA REPAIR ASSOCIATED), BRCA2 (BRCA2, DNA REPAIR ASSOCIATED) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; 185DELAG, 5385INSC, 6174DELT VARIANTS
81215	BRCA1 (BRCA1, DNA REPAIR ASSOCIATED) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; KNOWN FAMILIAL VARIANT
81216	BRCA2 (BRCA2, DNA REPAIR ASSOCIATED) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
81217	BRCA2 (BRCA2, DNA REPAIR ASSOCIATED) (EG, HEREDITARY BREAST AND OVARIAN CANCER) GENE ANALYSIS; KNOWN FAMILIAL VARIANT
81288	MLH1 (MUTL HOMOLOG 1, COLON CANCER, NONPOLYPOSIS TYPE 2) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; PROMOTER METHYLATION ANALYSIS

81292	MLH1 (MUTL HOMOLOG 1, COLON CANCER, NONPOLYPOSIS TYPE 2) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
81293	MLH1 (MUTL HOMOLOG 1, COLON CANCER, NONPOLYPOSIS TYPE 2) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; KNOWN FAMILIAL VARIANTS
81294	MLH1 (MUTL HOMOLOG 1, COLON CANCER, NONPOLYPOSIS TYPE 2) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; DUPLICATION/DELETION VARIANTS
81295	MSH2 (MUTS HOMOLOG 2, COLON CANCER, NONPOLYPOSIS TYPE 1) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
81296	MSH2 (MUTS HOMOLOG 2, COLON CANCER, NONPOLYPOSIS TYPE 1) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; KNOWN FAMILIAL VARIANTS
81297	MSH2 (MUTS HOMOLOG 2, COLON CANCER, NONPOLYPOSIS TYPE 1) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; DUPLICATION/DELETION VARIANTS
81298	MSH6 (MUTS HOMOLOG 6 [E. COLI]) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
81299	MSH6 (MUTS HOMOLOG 6 [E. COLI]) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; KNOWN FAMILIAL VARIANTS
81300	MSH6 (MUTS HOMOLOG 6 [E. COLI]) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; DUPLICATION/DELETION VARIANTS
81317	PMS2 (POSTMEIOTIC SEGREGATION INCREASED 2 [S. CEREVISIAE]) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
81318	PMS2 (POSTMEIOTIC SEGREGATION INCREASED 2 [S. CEREVISIAE]) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; KNOWN FAMILIAL VARIANTS
81319	PMS2 (POSTMEIOTIC SEGREGATION INCREASED 2 [S. CEREVISIAE]) (EG, HEREDITARY NON-POLYPOSIS COLORECTAL CANCER, LYNCH SYNDROME) GENE ANALYSIS; DUPLICATION/DELETION VARIANTS
81321	PTEN (PHOSPHATASE AND TENSIN HOMOLOG) (EG, COWDEN SYNDROME, PTEN HAMARTOMA TUMOR SYNDROME) GENE ANALYSIS; FULL SEQUENCE ANALYSIS
81322	PTEN (PHOSPHATASE AND TENSIN HOMOLOG) (EG, COWDEN SYNDROME, PTEN HAMARTOMA TUMOR SYNDROME) GENE ANALYSIS; KNOWN FAMILIAL VARIANT
81323	PTEN (PHOSPHATASE AND TENSIN HOMOLOG) (EG, COWDEN SYNDROME, PTEN HAMARTOMA TUMOR SYNDROME) GENE ANALYSIS; DUPLICATION/DELETION VARIANT

Thank you again for the opportunity to review and comment on this proposed policy. We are happy to provide additional information regarding our comments. Please direct your correspondence to Tara Burke, AMP Director of Public Policy, at tburke@amp.org or Nonda Wilson, CAP's Manager, Economic and Regulatory Affairs, at nwilson@cap.org.

Sincerely,

Association for Molecular Pathology
College of American Pathologists

References

1. Local Coverage Determination (LCD): MolDX: BRCA1 and BRCA2 Genetic Testing (L36082). Revision Effective Date 04/29/2021. Centers for Medicare & Medicaid Services Coverage Database. CMS.gov.

2. Local Coverage Article: Billing and Coding: MolDX: BRCA1 and BRCA2 Genetic Testing (A56854). Revision Effective Date 04/29/2021. Centers for Medicare & Medicaid Services Coverage Database. CMS.gov.

3. Local Coverage Determination (LCD): MolDX: Genetic testing for Lynch Syndrome (L35024). Revision Effective Date 01/07/2021. Centers for Medicare & Medicaid Services Coverage Database. CMS.gov.

4. Local Coverage Article: Billing and Coding: MolDX: Genetic Testing for Lynch Syndrome (A54987). Revision Effective Date 12/10/2020. Centers for Medicare & Medicaid Services Coverage Database. CMS.gov.

5. Local Coverage Determination (LCD): MolDX: Repeat Germline Testing (L38274). Effective Date 05/31/2020. Centers for Medicare & Medicaid Services Coverage Database. CMS.gov.

6. Local Coverage Article: Billing and Coding: MolDX: Repeat Germline Testing (A58017). Effective Date 05/31/2020. Centers for Medicare & Medicaid Services Coverage Database. CMS.gov.