ASSOCIATION FOR MOLECULAR PATHOLOGY
Providing global expertise in molecular testing that drives patient care
6120 Executive Boulevard, Suite 700, Rockville, Maryland, 20852
Tel: 301-634-7987 | Fax: 301-634-7995 | amp@amp.org | www.amp.org

November 15th, 2024

National Government Services Medical Policy Unit
P.O. Box 7108
Indianapolis, IN 46207-7108
NGSDraftLCDComments@anthem.com

Re: dLCD Genomic Sequence Analysis Panels in the Treatment of Hematolymphoid Diseases

Dear Medical Director,

On behalf of the Association for Molecular Pathology (AMP), thank you for the opportunity to submit comments on the dCLD Genomic Sequence Analysis Panels in the Treatment of Hematolymphoid Diseases DL 37606. AMP is an international medical and professional association representing approximately 3100 physicians, doctoral scientists, and medical technologists involved with laboratory testing based on knowledge derived from molecular biology, genetics, and genomics. Our membership includes professionals from the government, academic medicine, private and hospital-based clinical laboratories, and the in vitro diagnostics industry. AMP members are experts in molecular pathology and regularly perform this type of testing.

AMP would like to thank you for your approach to coverage in this policy. We believe that the updated genomic biomarkers will ensure patients with acute myelogenous leukemia (AML), myelodysplastic syndromes (MDS), and myeloproliferative neoplasms (MPN) will have access to the molecular testing necessary to guide their treatment.

However, AMP has a few recommendations to strengthen patient access to this type of testing.

Bibliography

AMP has a few concerns about the content of the bibliography. The synopsis of changes states that a reconsideration request was initiated because the previous version of the Local Coverage Determination (LCD) did not align with the updated diagnostic criteria of the World Health Organization (WHO), National Comprehensive Cancer Network (NCCN), and the International Consensus Classification (ICC). However, the bibliography does not reflect these updated reference guidelines. Because of this, AMP has the following suggestions for the applicable bibliographies included within the dLCD.

Acute Myelogenous Leukemia

Citations 5, 6, and 10 do not reflect current guideline recommendations and require updating. Below are AMP's recommendations for updating your citations.

Citation #5 within the dLCD	Updated Citation

Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood.* 2016 127:2391-2405; doi:10.1182/blood-2016-03-643544.	Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, Bejar R, Berti E, Busque L, Chan JKC, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. Leukemia. 2022 Jul;36(7):1703-1719. doi: 10.1038/s41375-022-01613-1. Epub 2022 Jun 22. PMID: 35732831

Citation #6 within the dLCD	Updated Citation
NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia Version 2.2016. Available at http://www.nccn.org/professionals/physician_gls/pdf/aml.pdf. Accessed: September 9, 2016	NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) NCCN Evidence BlocksTM Version 3.2024, 05/17/2024 © 2024 National Comprehensive Cancer Network® (NCCN®), All rights reserved. NCCN Evidence Blocks™, NCCN Guidelines®.

Citation #10 within the dLCD	Updated Citation
Cree IA, Alaggio R, Amador C, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Lymphoid Neoplasms. Leukemia. 2022;36(XX):XXXX-XXXX. doi:10.1038/s41375-022-01620-2	Alaggio et al. PMID 35732829 https://pubmed.ncbi.nlm.nih.gov/35732829/

Myelodysplastic Syndromes

Citations 1 and 2 do not reflect current guideline recommendations and require updating. Please see AMP's recommendations below.

Citation #1 within the dLCD	Updated Citation
Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood.* 2016 127:2391-2405; doi:10.1182/blood-2016-03-643544	Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, Bejar R, Berti E, Busque L, Chan JKC, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. Leukemia. 2022 Jul;36(7):1703-1719. doi: 10.1038/s41375-022-01613-1. Epub 2022 Jun 22. PMID: 35732831

Citation #2 within the dLCD	Updated Citation
National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms. Version 2.2017. Available at	NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Version 3.2024, 08/26/24 © 2024 National Comprehensive Cancer Network® (NCCN®), All rights reserved. NCCN Evidence Blocks™, NCCN

https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf. Accessed: Dec 21, 2016	Guidelines®. NCCN Evidence Blocks ™ Myelodysplastic Syndromes Version 3.2024 — August 26, 2024

Myeloproliferative Neoplasms

Citations 1 and 2 do not reflect current guideline recommendations and require updating. Please see AMP's recommendations below.

Citation #1 within the dLCD	Updated Citation
Mesa R, Jamieson C, Bhatia R, et al. Myeloproliferative Neoplasms. NCCN Clinical Practice Guidelines in Oncology. 2017;Version 2.2018.	NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Version 3.2024, 08/26/24 © 2024 National Comprehensive Cancer Network® (NCCN®), All rights reserved. NCCN Evidence Blocks™, NCCN Guidelines®. NCCN Evidence Blocks ™ Myelodysplastic Syndromes Version 3.2024 — August 26, 2024

Citation #2 within the dLCD	Updated Citation
Arber DA, Orazi A, Hasserjian R, et al. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. *Blood*. 2016;127(20):2391-2405.	Khoury JD, Solary E, Abla O, Akkari Y, Alaggio R, Apperley JF, Bejar R, Berti E, Busque L, Chan JKC, et al. The 5th edition of the World Health Organization Classification of Haematolymphoid Tumours: Myeloid and Histiocytic/Dendritic Neoplasms. Leukemia. 2022 Jul;36(7):1703-1719. doi: 10.1038/s41375-022-01613-1. Epub 2022 Jun 22. PMID: 35732831

Acute Myelogenous Leukemia

Coverage Indications

AMP recognizes that the covered indication was updated from the previous LCD and would like to add recommendations. AMP seeks clarification on the specific genes required for a testing panel to determine treatment for patients with AML. Furthermore, NCCN guidelines recommend NGS and Multiplex gene panel testing for the ongoing management of patients with AML. AMP recommends that the dLCD explicitly state that germline testing is covered withing this policy. The current terminology used is vague and does not clarify the usage of germline testing.

AMP also believes that Minimal Residual Disease (MRD) testing is important to monitor disease and best determine if a treatment is working. It has been proven that MRD testing directly impacts survival outcomes of patients with AML[1]. Due to this association, AMP recommends the inclusion of explicit language to account for MRD testing in patients.

[1] Short NJ, Zhou S, Fu C, Berry DA, Walter RB, Freeman SD, Hourigan CS, Huang X, Nogueras Gonzalez G, Hwang H, Qi X, Kantarjian H, Ravandi F. Association of Measurable Residual Disease With Survival Outcomes in Patients With Acute Myeloid Leukemia: A Systematic Review and Meta-analysis. JAMA Oncol. 2020 Dec 1;6(12):1890-1899. doi: 10.1001/jamaoncol.2020.4600. PMID: 33030517; PMCID: PMC7545346.

Analysis of Evidence

The biomarkers below, included in NCCN guidelines, aid in the treatment of patients with AML. As such, AMP requests that these additional biomarkers be added to Table 1, "Biomarkers that require a molecular diagnostics method (either via panel or individually)":

Table 1: Biomarkers associated with Blastic Plasmacytoid Dendritic Cell Neoplasm" (BPDCN)

Gene	Alteration	Clinical Utility	NCCN Biomarkers Category
TET2	Mutations	Poor Risk	2A
NRAS	Mutation	Poor Risk	2A
FLT3 TKD	Mutation	Intermediate	2A

Thank you for the opportunity to provide comments on the dCLD Genomic Sequence Analysis Panels in the Treatment of Hematolymphoid Diseases. We also attended your open meeting on this dLCD and would like to offer AMP as a resource and subject matter expert in the development future policies. We remain committed to working with you to ensure accurate pricing and secure patient access to laboratory tests. Should you have any questions or require additional information from AMP members, please contact Annie Scrimenti, Associate Director of Public Policy and Advocacy, at ascrimenti@amp.org.

Sincerely,

Maria E. Arcila, MD

President, Association for Molecular Pathology