Medica Central Coverage Policy

Policy Name:	**Genetic Testing – Oncology Testing: Hematologic Malignancy Molecular Diagnostics MP9797**
Effective Date:	**01/01/2026**

Important Information – Please Read Before Using This Policy

These services may or may not be covered by all Medica Central plans. Coverage is subject to requirements in applicable federal or state laws. Please refer to the member's plan document for other specific coverage information. If there is a difference between this general information and the member's plan document, the member's plan document will be used to determine coverage. With respect to Medicare, Medicaid, and other government programs, this policy will apply unless these programs require different coverage.

Members may contact Medica Customer Service at the phone number listed on their member identification card to discuss their benefits more specifically. Providers with questions may call the Provider Service Center. Please use the Quick Reference Guide on the Provider Communications page for the appropriate phone number. https://mo-central.medica.com/Providers/SSM-employee-health-plan-for-IL-MO-OK-providers

Medica Central coverage policies are not medical advice. Members should consult with appropriate health care providers to obtain needed medical advice, care, and treatment.

OVERVIEW

This policy addresses the use of diagnostic testing related to malignancies of the hematologic system.

While the primary goal of this testing is to identify biomarkers that diagnose cancer, or give prognostic and treatment selection information, this testing also has the potential to uncover clinically relevant germline variations that are associated with a hereditary cancer susceptibility syndrome, and other conditions, if confirmed to be present in the germline. Providers should communicate the potential for these incidental findings with their patients prior to somatic mutation profiling.

For additional information see the Rationale and References section.

The tests, CPT codes, and ICD codes referenced in this policy are not comprehensive, and their inclusion does not represent a guarantee of coverage or non-coverage. Please see the Concert Platform for additional registered tests.

POLICY REFERENCE TABLE

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
Molecular Profiling Panels for Hematologic Malignancies			

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
Broad RNA Fusion Panels for Hematologic Malignancy	Tempus xR Whole Transcriptome RNA Sequencing (Hematologic Malignancy) (Tempus, Inc.)	81456, C00-C80	Rationale/ References
Broad Molecular Profiling Panels For Hematologic Malignancies and Myeloid Malignancy Panels	FoundationOne Heme (Foundation Medicine)	81450, 81455, C91, C92, D46.9	Rationale/ References
	Tempus xT Hematologic Malignancy (Tempus, Inc.)		
	Neo Comprehensive - Myeloid Disorders (NeoGenomics Laboratories)		
	MayoComplete Myeloid Neoplasms, Comprehensive OncoHeme Next-Generation Sequencing, Varies (Mayo Clinic Laboratories)		
	Onkosight Advanced NGS Myeloid Panel (BioReference Laboratories)		
Acute Myeloid Leukemia (AML) Focused Molecular Profiling Panels	MyAML NGS Gene Panel Assay 0050U - (Laboratory for Personalized Molecular Medicine)	81450, 0050U, C92, D47	Rationale/ References
	NeoTYPE AML Prognostic Profile (NeoGenomics Laboratories)		
	LeukoVantage, Acute Myeloid Leukemia (AML) (Quest Diagnostics)		
Myeloproliferative Neoplasms (MPNs) Panels	Myeloproliferative Neoplasm, JAK2 V617F with Reflex to CALR and MPL, Varies (Mayo Clinic Laboratories)	81206, 81207, 81208, 81219, 81270, 81279, 81338, 81339, D47	Rationale/ References
	OnkoSight Advanced NGS JAK2, MPL, CALR Panel (BioReference Laboratories)		

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
Measurable (Minimal) Residual Disease (MRD) Analysis for Hematologic Malignancies			
Hematologic Minimal Residual Disease (MRD) Testing	MyMRD NGS Gene Panel Assay - 0171U (Laboratory for Personalized Molecular Medicine)	81218, 81272, 81455, 81456, 0171U, 0364U, 0450U, 0451U, C91, R71, R79	Rationale/ References
	ClonoSEQ Tracking (MRD) Assay - 0364U (Adaptive Biotechnologies)		
	M-inSight Patient Definition Assay - 0450U (Corgenix Clinical Laboratory)		
	M-inSight Patient Follow-Up Assessment - 0451U (Corgenix Clinical Laboratory)		
Single Gene Testing for Hematologic Malignancies			
Tumor Specific *BCR-ABL1* Kinase Domain Analysis	ABL1 Kinase Domain Mutation Analysis (NeoGenomics Laboratories)	81170, C91, C92	Rationale/ References
	Onkosight NGS ABL1 Sequencing (BioReference Laboratories)		
Tumor Specific *BCR-ABL1* FISH, Qualitative, and Quantitative Tests	BCR-ABL1 Gene Rearrangement, Quantitative, PCR (Quest Diagnostics)	81206, 81207, 81208, 81479, 88271, 88274, 88275, 88291, 0016U, 0040U, C83, C85, C91.00 - C91.02, C92.0 - C92.12, D45, D47, D47.1, D47.3, D69.3	Rationale/ References
	BCR-ABL1 Transcript Detection for Chronic Myelogenous Leukemia (CML) and Acute Lymphocytic Leukemia (ALL), Quantitative (LabCorp)		
	BCR/ABL1 (T9;22)) RNA Quantitative with Interpretation - 0016U (University of Iowa Hospitals and Clinics - Department of		

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
	Pathology)		
	MRDx BCR-ABL Test - 0040U (MolecularMD)		
	BCR/ABL/ASS1 t(9;22) (NeoGenomics Laboratories)		
	BCR ABL Qualitative (Cincinnati Children's Hospital)		
Tumor Specific *CALR* Variant Analysis	Calreticulin (CALR) Mutation Analysis (Quest Diagnostics)	81219, C94, D47.1	Rationale/ References
Tumor Specific *CEBPA* Variant Analysis	CEBPA Mutation Analysis (LabCorp)	81218, C92	Rationale/ References
Tumor Specific *FLT3* Variant Analysis	FLT3 ITD and TKD Mutation (PCR) (PathGroup)	81245, 81246, 0023U, 0046U, C92	Rationale/ References
	LeukoStrat CDx FLT3 Mutation Assay - 0023U (LabPMM LLC, an Invivoscribe Technologies, Inc Company)		
	FLT3 ITD MRD Assay - 0046U (LabPMM LLC, an Invivoscribe Technologies, Inc Company)		
Tumor Specific *IDH1* and *IDH2* Variant Analysis (Hematologic)	IDH1/IDH2 Mutation, Blood/Bone marrow (Cleveland Clinic Laboratories)	81120, 81121, C92, D47	Rationale/ References
Tumor Specific *IGHV* Somatic Hypermutation Analysis	IgVH Mutation Analysis (NeoGenomics Laboratories)	81261, 81262, 81263, C83, C91, D47.Z1	Rationale/ References
Tumor Specific *JAK2* Variant Analysis	JAK2 Exon 12 to 15 Sequencing, Polycythemia Vera Reflex, Varies - 0027U	81270, 81279, 0017U, 0027U, C91, C92, C94, D45, D47.1, D47.3,	Rationale/ References

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
	(Mayo Clinic Laboratories)	D75.81	
	JAK2 Mutation - 0017U (University of Iowa)		
	JAK2 V617F Mutation Analysis (Quest Diagnostics)		
Tumor Specific *KIT* Variant Analysis for Hematologic Malignancies	c-KIT Mutation Analysis (LabCorp)	81272, 81273, D47.02, C92.90	Rationale/ References
	KIT D816 Mutation Analysis (Mastocytosis) (Quest Diagnostics)		
Tumor Specific *MPL* Variant Analysis	MPL Mutation Analysis (Quest Diagnostics)	81338, 81339, D45, D47.1, D47.3, D75.81	Rationale/ References
Tumor Specific *NPM1* Variant Analysis	NPM1 MRD Assay - 0049U (Laboratory for Personalized Molecular Medicine)	81310, 0049U, C92	Rationale/ References
	Onkosight NGS NPM1 Sequencing (BioReference Laboratories)		
NTRK Fusion Analysis Panel for Hematologic Malignancies	NTRK Gene Fusion Panel, Tumor (Mayo Clinical Laboratories)	81194, C91.0	Rationale/ References
Tumor Specific *TP53* Variant Analysis	TP53 Mutation Analysis (NeoGenomics Laboratories)	81351, 81352, C92, R71, R79	Rationale/ References
Cytogenetic Testing for Hematologic Malignancies			
Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) FISH Panel Analysis	FISH for Chronic Lymphocytic Leukemia (Cleveland Clinic Laboratories)	88237, 88271, 88274, 88275, 88291, C91, C94, C95, Z85.6	Rationale/ References
	FISH, B-Cell Chronic Lymphocytic Leukemia Panel (Quest Diagnostics)		
Multiple Myeloma FISH Panel Analysis	Oncology FISH Analysis - Multiple Myeloma FISH Panel (Baylor Genetics, LLC)	88237, 88271, 88275, 88291, C90	Rationale/ References

COVERAGE CRITERIA SECTIONS	EXAMPLE TESTS (LABS)	COMMON BILLING CODES	SUPPORT
	Multiple Myeloma (MM) Profile, FISH (LabCorp)		
Tumor Specific *PML/RARA* Gene Rearrangement (Qualitative FISH and PCR)	FISH, APL, PML/RARA, Translocation 15, 17 (Quest Diagnostics)	81315, 81316, 88271, 88274, 88275, 88291, C91, C92, C93, C94, C95	Rationale/ References
	PML/RARA t(15;17) (NeoGenomics Laboratories)		
Red Blood Cell Genotyping in Multiple Myeloma			
Red Blood Cell Genotyping in Multiple Myeloma	PreciseType HEA - 0001U (Immucor)	0001U, 0180U, 0221U, C90.0, R71, R79	Rationale/ References
	Navigator ABO Sequencing - 0180U (Grifols Immunohematology Center)		
	Navigator ABO Blood Group NGS - 0221U (Grifols Immunohematology Center)		

RELATED POLICIES

This policy document provides coverage criteria for hematologic malignancy molecular diagnostics. Please refer to:

- ***Oncology Testing: Solid Tumor Molecular Diagnostics*** for coverage criteria related to molecular profiling of a known or suspected cancer (e.g., broad molecular profiling, including Minimal Residual Disease (MRD) Testing, Tumor Mutational Burden (TMB), and cytogenetic / fusion testing).
- ***Oncology Testing: Hereditary Cancer Susceptibility*** for coverage criteria related to genetic testing for hereditary cancer predisposition syndromes.
- ***Oncology Testing: Cancer Screening and Surveillance*** for coverage criteria related to screening and biomarker cancer tests.
- ***Oncology Testing: Algorithmic Assays*** for coverage criteria related to gene expression profiling and tumor biomarker tests with algorithmic analyses.
- ***Specialty Testing: Multisystem Genetic Conditions*** for coverage criteria related to diagnostic tests for genetic disorders that affect multiple organ systems (e.g., whole exome and genome sequencing, chromosomal microarray, and multigene panels for broad phenotypes).
- ***General Approach to Laboratory Testing*** for coverage criteria related to hematologic malignancies, including known familial variant testing, that is not specifically discussed in

this or another non-general policy.

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COVERAGE CRITERIA

MOLECULAR PROFILING PANELS FOR HEMATOLOGIC MALIGNANCIES

Broad RNA Fusion Panels for Hematologic Malignancy

I. RNA fusion panel tests with 51 or more genes utilizing RNA analysis alone that are performed on hematologic malignancies are considered **medically necessary** when:

   A. The member is undergoing diagnostic workup for adult or pediatric acute lymphoblastic leukemia (ALL).

II. RNA fusion panel tests with 51 or more genes utilizing RNA analysis alone that are performed on hematologic malignancies are considered **investigational** for all other indications.

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Broad Molecular Profiling Panels For Hematologic Malignancies and Myeloid Malignancy Panels

I. Broad molecular profiling panels for hematologic malignancies and myeloid malignancy panels in bone marrow or peripheral blood are considered **medically necessary** when:

   A. The member is undergoing evaluation for acute myeloid leukemia (AML), **OR**

   B. The member has newly diagnosed acute lymphoblastic leukemia (ALL), **OR**

   C. The member has newly diagnosed myelodysplastic syndrome (MDS), **OR**

   D. The member has suspected myelodysplastic syndrome (MDS) **AND**

      1. Other causes of cytopenia(s) have been ruled out, **OR**

   E. The member is suspected to have a myeloproliferative neoplasm (MPN), **AND**

      1. This is the member's initial genetic evaluation for suspected MPN, **OR**

      2. Previous results of *JAK2*, *CALR*, and *MPL* analysis were negative, **OR**

   F. The member has a diagnosis of chronic myelogenous leukemia (CML), **AND**

      1. There has been progression to accelerated or blast phase, **OR**

      2. Results of *BCR-ABL1* kinase domain mutation analysis were negative, **OR**

   G. The member has a diagnosis of diffuse large B-cell lymphoma.

II. Repeat broad molecular profiling panels for hematologic malignancies and myeloid malignancy panels in bone marrow or peripheral blood are considered **medically necessary** when:

A. The member has myelodysplastic syndrome (MDS), **AND**

1. The member has relapsed after allo-HCT (hematopoietic cell transplant), **OR**

B. The member has acute lymphoblastic leukemia (ALL), **AND**

1. The member is showing evidence of symptomatic relapse after maintenance therapy, **OR**

C. The member has acute myeloid leukemia (AML), **AND**

1. The member has relapsed or refractory disease after consolidation or progression on treatment.

III. Broad molecular profiling panels for hematologic malignancies and myeloid malignancy panels in bone marrow or peripheral blood are considered **investigational** for all other indications.

NOTE: If a multigene panel is performed, appropriate panel codes should be used. These clinical criteria are not intended to address liquid biopsies.

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Acute Myeloid Leukemia (AML) Focused Molecular Profiling Panels

I. Acute myeloid leukemia focused molecular profiling panels for the diagnosis or evaluation of acute myeloid leukemia (AML) are considered **medically necessary** when:

A. The member has a suspected or confirmed diagnosis of acute myeloid leukemia (AML).

II. Acute myeloid leukemia focused molecular profiling panels for the diagnosis or evaluation of acute myeloid leukemia (AML) are considered **investigational** for all other indications.

NOTE: If a multigene panel is performed, appropriate panel codes should be used.

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Myeloproliferative Neoplasms (MPNs) Panels

I. Myeloproliferative neoplasm (MPN) molecular profiling panels are considered **medically necessary** when:

A. The member is suspected to have a myeloproliferative neoplasm (MPN), **AND**

B. The panel includes, at a minimum, testing of the following genes: *JAK2*, *CALR*, and *MPL*.

II. Myeloproliferative neoplasm (MPN) molecular profiling panels are considered **investigational** for all other indications.

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MEASURABLE (MINIMAL) RESIDUAL DISEASE (MRD) ANALYSIS FOR HEMATOLOGIC MALIGNANCIES

Hematologic Minimal Residual Disease (MRD) Testing

I. Measurable (minimal) residual disease (MRD) analysis in bone marrow or peripheral blood is considered **medically necessary** when:

A. The member has a diagnosis of:

1. Acute Lymphocytic Leukemia (ALL), **OR**
2. Multiple Myeloma, **OR**
3. Diffuse Large B-Cell Lymphoma, **AND**
    a) The member has completed a treatment cycle**, OR**
4. Chronic Lymphocytic Leukemia (CLL), **AND**
    a) The member has completed treatment.

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SINGLE GENE TESTING FOR HEMATOLOGIC MALIGNANCIES

Tumor Specific *BCR-ABL1* Kinase Domain Analysis

I. Tumor specific *BCR-ABL1* kinase domain analysis in hematologic malignancies is considered **medically necessary** when:

A. The member has a diagnosis of any of the following:

1. Chronic myeloid leukemia (CML), **OR**
2. Ph-positive acute lymphocytic leukemia (ALL), **AND**

B. The member has any of the following:

1. Inadequate initial response to TKI therapy, **OR**
2. Loss of response to TKI therapy, **OR**
3. Disease progression to the accelerated or blast phase, **OR**
4. Relapsed/refractory disease.

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Tumor Specific *BCR-ABL1* FISH, Qualitative, and Quantitative Tests

I. Tumor specific *BCR-ABL1* FISH, qualitative, or quantitative tests in hematologic malignancies are considered **medically necessary** when:

A. The member is suspected to have a myeloproliferative neoplasm (MPN), **OR**

B. The member is undergoing diagnostic workup for:

1. Acute lymphoblastic leukemia (ALL), **OR**
2. Acute myeloid leukemia (AML), **OR**
3. Chronic myeloid leukemia (CML), **OR**
4. Lymphoblastic leukemia, **OR**

C. The member is undergoing monitoring of disease progression or for minimal residual disease (MRD) monitoring using a quantitative test only for:

1. Acute lymphoblastic leukemia (ALL), **OR**
2. Acute myeloid leukemia (AML), **OR**
3. Chronic myeloid leukemia (CML), **AND**

a) The member's provider is considering discontinuation of or has already discontinued use of TKI therapy.

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Tumor Specific *CALR* Variant Analysis

I. Tumor specific *CALR* variant analysis is considered **medically necessary** when:

A. The member is suspected to have a myeloproliferative neoplasm (MPN), **OR**

B. The member is suspected to have a myelodysplastic syndrome (MDS).

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Tumor Specific *CEBPA* Variant Analysis

I. Tumor specific *CEBPA* variant analysis in hematologic malignancies is considered **medically necessary** when:

A. The member is undergoing evaluation for acute myeloid leukemia (AML).

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Tumor Specific *FLT3* Variant Analysis

I. Tumor specific *FLT3* variant analysis in hematologic malignancies is considered **medically necessary** when:

A. The member has suspected or confirmed acute myeloid leukemia (AML), **OR**

B. The member has a diagnosis of:

1. Acute lymphocytic leukemia (ALL), **OR**
2. Myelodysplastic syndrome (MDS), **OR**
3. Myeloproliferative neoplasm (MPN).

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Tumor Specific *IDH1* and *IDH2* Variant Analysis (Hematologic)

I. Tumor specific *IDH1* and *IDH2* variant analysis in hematologic malignancies is considered **medically necessary** when:

A. The member has a diagnosis of acute myeloid leukemia (AML).

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Tumor Specific *IGHV* Somatic Hypermutation Analysis

I. Tumor specific *IGHV* somatic hypermutation analysis in hematologic malignancies is considered **medically necessary** when:

A. The member is undergoing work up for or has a diagnosis of:

1. Chronic lymphocytic leukemia (CLL), **OR**
2. Small lymphocytic leukemia (SLL), **OR**
3. Primary cutaneous B-cell lymphoma, **OR**
4. B-cell lymphoma.

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Tumor Specific *JAK2* Variant Analysis

I. Tumor specific *JAK2* variant analysis in hematologic malignancies is considered **medically necessary** when:

A. The member is suspected to have a myeloproliferative neoplasm (MPN), **OR**

B. The member has acute lymphoblastic leukemia (ALL), **OR**

C. The member is suspected to have a myelodysplastic syndrome (MDS).

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Tumor Specific *KIT* Variant Analysis for Hematologic Malignancies

I. Tumor specific *KIT* variant analysis in hematologic malignancies is considered **medically necessary** when:

A. The member is being evaluated for systemic mastocytosis, **OR**

B. The member has a diagnosis of acute myeloid leukemia (AML).

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Tumor Specific *MPL* Variant Analysis

I. Tumor specific *MPL* variant analysis in hematologic malignancies is considered **medically necessary** when:

A. The member is suspected to have a myeloproliferative neoplasm (MPN), **OR**

B. The member is suspected to have a myelodysplastic syndrome (MDS).

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Tumor Specific *NPM1* Variant Analysis

I. Tumor specific *NPM1* variant analysis in hematological malignancies is considered **medically necessary** when:

A. The member is undergoing evaluation for acute myeloid leukemia (AML).

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***NTRK* Fusion Analysis Panel for Hematologic Malignancies**

I. *NTRK 1/2/3* fusion analysis panel via fluorescent in situ hybridization (FISH) or immunohistochemistry (IHC) in hematologic malignancies is considered **medically necessary** when:

A. The member has a diagnosis of any of the following cancers at any stage:

1. Acute lymphoblastic leukemia (ALL).

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Tumor Specific *TP53* Variant Analysis

I. Tumor specific *TP53* variant analysis in bone marrow or peripheral blood is considered **medically necessary** when:

A. The member has a diagnosis of:

1. Acute myeloid leukemia (AML), **OR**
2. Chronic lymphocytic leukemia (CLL), **OR**
3. Small lymphocytic leukemia (SLL), **OR**

B. The member is undergoing diagnostic workup for:

1. Mantle cell lymphoma (MCL), **OR**
2. Multiple myeloma.

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CYTOGENETIC TESTING FOR HEMATOLOGIC MALIGNANCIES

Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) FISH Panel Analysis

I. Chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL) FISH panel analysis in peripheral blood or bone marrow is considered **medically necessary** when:

A. The member is undergoing initial diagnostic workup for chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL).

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Multiple Myeloma FISH Panel Analysis

I. Multiple myeloma FISH panel analysis of bone marrow is considered **medically necessary** when:

A. The panel includes analysis for del(13), del(17p13), t(4;14), t(11;14), t(14;16), t(14;20), 1q21 gain/amplification, and del(1p), **AND**

B. The member is undergoing initial diagnostic workup for multiple myeloma.

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Tumor Specific *PML*/*RARA* Gene Rearrangement (Qualitative FISH and PCR)

I. *PML/RARA* rearrangement analysis via fluorescent in situ hybridization (FISH) in peripheral blood or bone marrow is considered **medically necessary** when:

A. The member is undergoing initial diagnostic work up for acute myeloid leukemia

(AML).

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RED BLOOD CELL GENOTYPING IN MULTIPLE MYELOMA

Red Blood Cell Genotyping in Multiple Myeloma

I. Red blood cell genotyping in individuals with multiple myeloma is considered **medically necessary** when:

   A. The member has a diagnosis of multiple myeloma, **AND**

   B. The member is currently being treated or will be treated with an anti-CD38 monoclonal antibody.

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PRIOR AUTHORIZATION

Prior authorization is not required. However, services with specific coverage criteria may be reviewed retrospectively to determine if criteria are being met. Retrospective denial may result if criteria are not met.

RATIONALE AND REFERENCES

Broad RNA Fusion Panels for Hematologic Malignancy

National Comprehensive Cancer Network (NCCN): Acute Lymphoblastic Leukemia (2.2025)

This guideline recommends comprehensive testing by next-generation sequencing (NGS) for gene fusions and pathogenic mutations at the time of diagnosis (p. ALL-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/all.pdf

National Comprehensive Cancer Network (NCCN): Pediatric Acute Lymphoblastic Leukemia (3.2025)

This guideline recommends testing for potentially actionable or prognostic mutations and gene fusions via next generation sequencing (NGS) or alternative methods at the time of diagnosis (p. PEDALL-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia 3.2025
https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf

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Broad Molecular Profiling Panels For Hematologic Malignancies and Myeloid Malignancy Panels

National Comprehensive Cancer Network (NCCN): Acute Myeloid Leukemia (2.2025)

This guideline recommends molecular testing via multiplex gene panels and targeted analysis by next generation sequencing for adult patients for purposes of prognostication, therapy, ongoing management (p. EVAL-1, EVAL-2A), and in the presence of relapsed or refractory disease after completion of consolidation (p. AML-8, AML-J 1 of 2).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf

National Comprehensive Cancer Network (NCCN): Acute Lymphoblastic Leukemia (2.2025)

This guideline recommends that patients diagnosed with acute lymphoblastic leukemia should undergo molecular characterization of their disease, including comprehensive testing for gene fusions and pathogenic mutations (p. ALL-1). Additionally, patients who are undergoing surveillance after maintenance therapy and are showing evidence of symptomatic relapse should undergo repeat testing (p. ALL-8).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/all.pdf

National Comprehensive Cancer Network (NCCN): Myelodysplastic Syndromes (2.2025)

This guideline recommends molecular testing during the initial evaluation of suspected myelodysplasia in patients with cytopenia. Testing should be performed on bone marrow or peripheral blood for somatic mutations in genes associated with myelodysplastic syndromes (p. MDS-1, MDS-1A).

Repeat molecular testing is appropriate if a patient has relapsed after allo-HCT (hematopoietic cell transplant (p. MDS-7 and MDS-7A).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf

National Comprehensive Cancer Network (NCCN): Myeloproliferative Neoplasms (2.2025)

This guideline recommends molecular testing on blood or bone marrow for patients suspected of having a myeloproliferative neoplasm. This testing can be done in a stepwise manner, or as an NGS multigene panel that includes *JAK2*, *CALR* and *MPL*. Once a diagnosis is confirmed, additional testing for somatic mutations is recommended for prognostication (p. MPN-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf

National Comprehensive Cancer Network (NCCN): Chronic Myeloid Leukemia (1.2026)

This guideline recommends consideration of testing for myeloid mutations for patients with advanced phase CML who are in either accelerated or blast phase (CML-1). NCCN recommends consideration of panel testing for myeloid mutations in patients on TKI therapy who have progressed to accelerated or blast phase if they lack a *BCR-ABL1* kinase domain mutation (p. CML-E).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Chronic Myeloid Leukemia 1.2026 https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf

National Comprehensive Cancer Network (NCCN): B-Cell Lymphomas (2.2025)

This guideline recommends consideration of an NGS panel (BCEL-1), to include at a minimum more than 50 genes with known clinical association (BCEL-A 1 of 3).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: B-Cell Lymphomas 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf

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Acute Myeloid Leukemia (AML) Focused Molecular Profiling Panels

National Comprehensive Cancer Network (NCCN): Acute Myeloid Leukemia (2.2025)

This guideline recommends molecular testing via multiplex gene panels and targeted analysis by next generation sequencing for adult patients for purposes of prognostication, therapy, and ongoing management (p. EVAL-1, EVAL-2A).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf

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Myeloproliferative Neoplasms (MPNs) Panels

National Comprehensive Cancer Network (NCCN): Myeloproliferative Neoplasms (2.2025)

This guideline recommends molecular testing in the workup phase for myeloproliferative neoplasms. Molecular testing using a multigene NGS panel that includes at least *JAK2, MPL* and *CALR* can be used as an alternative to stepwise single gene testing (p. MPN-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf

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Hematologic Minimal Residual Disease (MRD) Testing

National Comprehensive Cancer Network (NCCN): Acute Lymphoblastic Leukemia (2.2025)

This guideline recommends minimal residual disease (MRD) testing at numerous time points including prior to induction, following consolidation therapy, for serial monitoring, and as needed based on regimen and risk factors. MRD may also be used at baseline if needed for characterization of the leukemic clone to be used in subsequent MRD analysis (p. ALL-1, ALL-F).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/all.pdf

National Comprehensive Cancer Network (NCCN): Multiple Myeloma (2.2026)

This guideline recommends consideration of a baseline clone identification and storage of an aspirate sample for MRD testing by NGS in the initial diagnostic workup (p. MYEL-1), prognostication during follow up after primary treatment (p. MYEL-4), and as part of response assessment after suspected complete response following each stage of treatment and prior to starting a new therapy (p. MYEL-E 1 of 3, MYEL-E 3 of 3).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma 2.2026
https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf

National Comprehensive Cancer Network (NCCN): Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (3.2025)

This guideline recommends minimal residual disease testing at the end of treatment for CLL/SLL as an important predictor of treatment effectiveness. MRD evaluation can be done using flow cytometry, PCR or NGS assay (p. CSLL-E, 2 of 2).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma 3.2025
https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf

National Comprehensive Cancer Network (NCCN): B-Cell Lymphomas (2.2025)

This guideline recommends consideration of MRD testing to determine the potential need for additional therapy in several scenarios:

- For stage I-II diffuse large B-cell lymphoma (DLBCL) assessment of end-of treatment-response when PET is positive and biopsy is not feasible (p. BCEL-4),
- For stage I-II DLBCL during restaging and additional therapy planning when PET is positive and biopsy is not feasible (p. BCEL-5), and
- For extensive Stage I-II not treatable by radiation therapy or any stage III-IV DLCBL when PET is positive and biopsy is not feasible (p. BCEL-6)

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: B-Cell Lymphomas 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf

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Tumor Specific *BCR-ABL1* Kinase Domain Analysis

National Comprehensive Cancer Network (NCCN): Chronic Myeloid Leukemia (1.2026)

This guideline recommends *BCR-ABL1* kinase domain testing for diagnosis and monitoring of chronic myelogenous leukemia. Specifically, *BCR-ABL1* kinase domain mutational analysis is recommended when patients fail to meet treatment milestones (inadequate response) (p.CML-3), when patients show any sign of loss of response (hematologic or cytogenetic relapse), and when there is a 1-log increase in *BCR-ABL1* transcript levels with loss of major molecular response (MMR). Additionally, this test is recommended with disease progression to accelerated phase or blast phase (p. CML-G).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Chronic Myeloid Leukemia 1.2026 https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf

National Comprehensive Cancer Network (NCCN): Acute Lymphoblastic Leukemia (2.2025)

This guideline recommends *ABL1* kinase domain mutation testing for patients with relapsed/refractory, Philadelphia chromosome positive (Ph+) B-ALL (p. ALL-9) acute lymphoblastic leukemia.

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/all.pdf

National Comprehensive Cancer Network (NCCN): Pediatric Acute Lymphoblastic Leukemia (3.2025)

This guideline recommends *ABL1* kinase domain mutation testing for patients with “B-ALL first relapse disease” (p. PEDALL-9).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia 3.2025 https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf

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Tumor Specific *BCR-ABL1* FISH, Qualitative, and Quantitative Tests

National Comprehensive Cancer Network (NCCN): Pediatric Acute Lymphoblastic Leukemia (3.2025)

This guideline recommends quantitative or qualitative reverse transcriptase-polymerase chain reaction (RT-PCR) testing for *BCR-ABL1* in B-ALL to determine transcript size (p. PEDALL-1).

Additionally, reverse transcriptase quantitative PCR assay of *BCR-ABL1* is used to assess minimal residual disease (p. PEDALL-J, 1 of 2).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia 3.2025
https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf

National Comprehensive Cancer Network (NCCN): Acute Lymphoblastic Leukemia (2.2025)

This guideline recommends reverse transcriptase-polymerase chain reaction (RT-PCR) testing for *BCR-ABL1* in B-ALL (quantitative or qualitative), including determination of transcript size (ie, p190 vs. p210) (p. ALL-1). Additionally, reverse transcriptase quantitative PCR (RT-qPCR) assays for *BCR-ABL1* are used to monitor minimal residual disease (p. ALL-F).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/all.pdf

National Comprehensive Cancer Network (NCCN): Myeloproliferative Neoplasms (2.2025)

This guideline recommends evaluation for *BCR-ABL1* via FISH or multiplex RT-PCR to exclude a diagnosis of CML (p. MPN-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf

National Comprehensive Cancer Network (NCCN): Acute Myeloid Leukemia (2.2025)

This guideline recommends molecular testing to assist with prognostication of AML in the evaluation and initial workup for suspected AML (p. EVAL-1 and AML-A). The NCCN guidelines also recommend confirmation of remission and ongoing monitoring for recurrence by PCR (p. APL-5).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf

National Comprehensive Cancer Network (NCCN): Chronic Myeloid Leukemia (1.2026)

This guideline recommends quantitative RT-PCR testing on blood for *BCR-ABL1* for patients undergoing work-up for CML. NCCN also recommends consideration of qualitative RT-PCR for the detection of atypical *BCR-ABL1* transcripts (p. CML-1). The NCCN guidelines also recommend confirmation of remission and ongoing monitoring for recurrence by PCR (p.CML-6). For discontinuation of TKI therapy, NCCN recommends that patients meet several criteria, including frequent molecular monitoring indefinitely to ensure remission (p. CML-H).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Chronic Myeloid Leukemia 1.2026
https://www.nccn.org/professionals/physician_gls/pdf/cml.pdf

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Tumor Specific *CALR* Variant Analysis

National Comprehensive Cancer Network (NCCN): Myeloproliferative Neoplasms (2.2025)

This guideline recommends molecular testing for *CALR* mutations in initial work-up for all patients with suspected MPN. Alternatively, molecular testing using a multigene NGS panel that includes *JAK2, MPL* and *CALR* can be used as part of the initial work-up in all patients (p. MPN-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf

National Comprehensive Cancer Network (NCCN): Myelodysplastic Syndromes (2.2025)

This guideline recommends genetic testing for somatic mutations in genes associated with MDS, which includes CALR (p. MDS-1, MDS-C 2 of 3, MDS-A 3 of 5).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf

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Tumor Specific *CEBPA* Variant Analysis

National Comprehensive Cancer Network (NCCN): Acute Myeloid Leukemia (2.2025)

This guideline recommends that molecular testing be part of the evaluation for AML for all patients and lists multiple gene mutations that might aid in prognosis, guide medical decision making, or therapeutic decisions. Presently this list of genes includes *CEBPA* (p. EVAL-1, EVAL-2A).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf

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Tumor Specific *FLT3* Variant Analysis

National Comprehensive Cancer Network (NCCN): Acute Myeloid Leukemia (2.2025)

This guideline recommends molecular testing be part of the evaluation for AML and lists multiple gene mutations that might aid in prognosis, guide medical decision making, or therapeutic decisions. Presently this list includes *FLT3* (p. EVAL-1, EVAL-2A).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf

National Comprehensive Cancer Network (NCCN): Acute Lymphoblastic Leukemia (2.2025)

This guideline recommends comprehensive testing for gene fusions and pathogenic mutations using NGS sequencing for molecular prognostic risk stratification and states that *FLT3* mutations confer poor or unfavorable risk (p. ALL-1, ALL-3).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/all.pdf

National Comprehensive Cancer Network (NCCN): Pediatric Acute Lymphoblastic Leukemia (3.2025)

This guideline recommends comprehensive testing for gene fusions and pathogenic mutations using NGS sequencing for molecular prognostic risk stratification and states that *FLT3* mutations confer poor or unfavorable risk (PEDALL-1, PEDALL-A, 1 of 2).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia 3.2025
https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf

National Comprehensive Cancer Network (NCCN): Myelodysplastic Syndromes (2.2025)

This guideline recommends that during initial evaluation for suspected myelodysplasia, genetic testing for somatic mutations in genes associated with myelodysplastic syndromes should be done, which includes *FLT3* (p. MDS-1, MDS-C 2 of 4).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf

National Comprehensive Cancer Network (NCCN): Myeloproliferative Neoplasms (2.2025)

This guideline recommends molecular testing via NGS panel for mutational prognostication in patients with confirmed MPN diagnosis (p. MPN-1). Based on NGS panel results (e.g., if NGS shows particular mutations such as *IDH1*, *IDH2*, or *FLT3*), low intensity or targeted therapy can be considered (p. MPN-AP/BP-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf

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Tumor Specific *IDH1* and *IDH2* Variant Analysis (Hematologic)

National Comprehensive Cancer Network (NCCN): Acute Myeloid Leukemia (2.2025)

This guideline recommends molecular testing during the initial evaluation for AML and lists *IDH1* and *IDH2* as genes to be included in analysis for prognosis and treatment decision making (p. EVAL-1, EVAL-2A).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf

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Tumor Specific *IGHV* Somatic Hypermutation Analysis

National Comprehensive Cancer Network (NCCN): Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (3.2025)

This guideline recommends molecular testing for the immunoglobulin heavy chain variable region gene (*IGHV*) as it is useful for prognostic and/or therapy determination (p. CSLL-1 and CSLL-A 1 of 5).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma 3.2025 https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf

National Comprehensive Cancer Network (NCCN): B-cell Lymphomas (2.2025)

This guideline recommends molecular analysis to detect Ig gene rearrangements (IGHV) during the diagnostic workup for B Cell lymphomas. Testing should be done on an excisional or incisional lymph node biopsy (p. DIAG-1, MS-3,4).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: B-Cell Lymphomas 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf

National Comprehensive Cancer Network (NCCN): Primary Cutaneous Lymphomas (3.2025)

This guideline recommends consideration of flow cytometry or IGH gene rearrangement studies for patients with primary cutaneous B-cell lymphoma to determine B-cell clonality, if adequate biopsy material is available (p. CUTB-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Primary Cutaneous Lymphomas 3.2025 https://www.nccn.org/professionals/physician_gls/pdf/primary_cutaneous.pdf

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Tumor Specific *JAK2* Variant Analysis

National Comprehensive Cancer Network (NCCN): Myeloproliferative Neoplasms (2.2025)

This guideline recommends molecular testing for *JAK2* mutations in the initial work-up for all patients with suspected MPN (p. MPN-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf

National Comprehensive Cancer Network (NCCN): Acute Lymphoblastic Leukemia (2.2025)

This guideline recommends cytogenetic and molecular prognostic risk stratification for B-ALL using comprehensive NGS testing (p. ALL-2 and 2A). Gene fusions and mutations that activate tyrosine kinase pathways are associated with Ph-like ALL and an unfavorable prognosis; these include gene fusions involving *JAK2*.

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/all.pdf

National Comprehensive Cancer Network (NCCN): Pediatric Acute Lymphoblastic Leukemia (3.2025)

This guideline recommends cytogenetic and molecular prognostic risk stratification for B-ALL using comprehensive NGS testing (PEDALL-1 and 1A). Gene fusions and mutations that activate tyrosine kinase pathways are associated with Ph-like ALL and an unfavorable prognosis; these include gene fusions involving *JAK2* (PEDALL-1A).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia 3.2025
https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf

National Comprehensive Cancer Network (NCCN): Myelodysplastic Syndromes (2.2025)

This guideline recommends genetic testing for somatic mutations in genes associated with MDS, which includes *JAK2* (p. MDS-1, MDS-C 2 of 4).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf

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Tumor Specific *KIT* Variant Analysis for Hematologic Malignancies

National Comprehensive Cancer Network (NCCN): Acute Myeloid Leukemia (2.2025)

This guideline recommends molecular testing during the evaluation for AML for genes associated with prognosis or treatment options, including *KIT* analysis (p. EVAL-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf

National Comprehensive Cancer Network (NCCN): Systemic Mastocytosis (1.2025)

This guideline recommends that all patients presenting with signs or symptoms of mastocytosis undergo molecular testing for *KIT* mutations (specifically, the *KIT* D816V mutation) (p. SM-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Systemic Mastocytosis 1.2025
https://www.nccn.org/professionals/physician_gls/pdf/mastocytosis.pdf

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Tumor Specific *MPL* Variant Analysis

National Comprehensive Cancer Network (NCCN): Myeloproliferative Neoplasms (2.2025)

This guideline recommends molecular testing (blood or bone marrow) for patients with suspicion of myeloproliferative disease. Testing can be done in a stepwise fashion or via a multigene panel that includes *JAK2*, *CALR* and *MPL* (p. MPN-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myeloproliferative Neoplasms 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/mpn.pdf

National Comprehensive Cancer Network (NCCN): Myelodysplastic Syndromes (2.2025)

This guideline recommends genetic testing for somatic mutations in genes associated with MDS, which includes MPL (p. MDS-1, MDS-C 2 of 3).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Myelodysplastic Syndromes 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/mds.pdf

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Tumor Specific *NPM1* Variant Analysis

National Comprehensive Cancer Network (NCCN): Acute Myeloid Leukemia (2.2025)

This guideline recommends molecular testing during the evaluation for AML for genes associated with prognosis or treatment options, including *NPM1* (p. EVAL-1, EVAL-2A).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia 2.2025
https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf

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NTRK Fusion Analysis Panel for Hematologic Malignancies

National Comprehensive Cancer Network (NCCN): Acute Lymphoblastic Leukemia (2.2025)

This guideline recommends *NTRK* fusion analysis for acute lymphoblastic leukemia (ALL) for the purposes of risk stratification (p. ALL-2).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Lymphoblastic Leukemia 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/all.pdf

National Comprehensive Cancer Network (NCCN): Pediatric Acute Lymphoblastic Leukemia (3.2025)

This guideline recommends NTRK fusion analysis for acute lymphoblastic leukemia (ALL) for the purposes of risk stratification (p. PEDALL-B).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Pediatric Acute Lymphoblastic Leukemia 3.2025 https://www.nccn.org/professionals/physician_gls/pdf/ped_all.pdf

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Tumor Specific *TP53* Variant Analysis

National Comprehensive Cancer Network (NCCN): Acute Myeloid Leukemia (2.2025)

This guideline recommends molecular testing during the evaluation for AML for genes with prognostic or treatment implications, including TP53 (p. EVAL-1, EVAL-2A).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Acute Myeloid Leukemia 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/aml.pdf

National Comprehensive Cancer Network (NCCN): B-Cell Lymphomas (2.2025)

This guideline recommends *TP53* mutation analysis for patients with a diagnosis of mantle cell lymphoma in order to direct treatment selection, as patients with a *TP53* mutation have been associated with poor prognosis when treated with conventional therapy (p. MANT-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: B-Cell Lymphomas 2.2025 https://www.nccn.org/professionals/physician_gls/pdf/b-cell.pdf

National Comprehensive Cancer Network (NCCN): Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (3.2025)

This guideline recommends *TP53* sequencing analysis to inform prognosis and therapeutic options for patients diagnosed with CLL/SLL or upon progression or recurrence (p. CSLL-1, CSLL-4A).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma 3.2025 https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf

National Comprehensive Cancer Network (NCCN): Multiple Myeloma (2.2026)

This guideline recommends *TP53* mutation analysis during the initial work-up for multiple myeloma (p. MYEL-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma 2.2026 https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf

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Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (CLL/SLL) FISH Panel Analysis

National Comprehensive Cancer Network (NCCN): Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma (3.2025)

This guideline recommends FISH testing including +12; del(11q); del(13q); del(17p) during the diagnostic workup for CLL/SLL and states this is "informative for prognostic and/or therapy determination" (p. CSLL-1, CSLL-A). Ruling out mantle cell lymphoma via FISH for t(11;14); t(11q;v) is recommended during the diagnostic workup when the initial diagnosis was made by flow cytometry (CSLL-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Chronic Lymphocytic Leukemia/Small Lymphocytic Lymphoma 3.2025 https://www.nccn.org/professionals/physician_gls/pdf/cll.pdf

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Multiple Myeloma FISH Panel Analysis

National Comprehensive Cancer Network (NCCN): Multiple Myeloma (2.2026)

This guideline recommends FISH testing during the initial workup of multiple myeloma for prognostic purposes. The recommended FISH testing includes: del(13), del (17p13), t(4;14), t(11;14), t(14;16), t(14:20), 1q21 gain/1q21 amplification, 1p deletion (p. MYEL-1).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma 2.2026 https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf

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Tumor Specific *PML/RARA* Gene Rearrangement (Qualitative FISH and PCR)

National Comprehensive Cancer Network (NCCN): Multiple Myeloma (2.2026)

This guideline states that many different types of gene mutations are associated with specific prognoses, helping to guide medical management decisions, and/or may indicate that specific therapeutic agents are useful. Therefore, all patients with AML should be tested for these

mutations (p. EVAL-1). The discussion section of this guideline states that *PML-RARA* alpha is included in this group of genetic markers that should be tested in all patients (p. MS-4).

National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Multiple Myeloma 2.2026
https://www.nccn.org/professionals/physician_gls/pdf/myeloma.pdf

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Red Blood Cell Genotyping in Multiple Myeloma

Association for the Advancement of Blood and Biotherapies (AABB)

The AABB (Association for the Advancement of Blood and Biotherapies; formerly known as the American Association of Blood Banks) published Association Bulletin #16-02 on January 15, 2016 (updated April 2024) recommending consideration of baseline phenotype and genotype prior to initiation of anti-CD38 monoclonal antibody treatment to mitigate the potential of anti-CD38 interference with serologic testing. The bulletin also notes that this genotyping can be performed after the initiation of treatment (p. 3).

Association for the Advancement of Blood and Biotherapies. Association Bulletin #16-02: Mitigating the Anti-CD38 Interference with Serologic Testing. Published January 15, 2016. Updated April 2024. https://www.aabb.org/docs/default-source/default-document-library/resources/association-bulletins/ab16-02.pdf

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DEFINITIONS

1. A **Myeloproliferative Neoplasm (MPN)** is a rare blood disease in which the bone marrow makes too many red blood cells, white blood cells, or platelets.There are seven subcategories of myeloproliferative neoplasms:
    a. Chronic myeloid leukemia (CML)
    b. Polycythemia vera (PV)
    c. Primary myelofibrosis (PMF)
    d. Essential thrombocytopenia (ET)
    e. Chronic neutrophilic leukemia
    f. Chronic eosinophilic leukemia
    g. Chronic eosinophilic leukemia-not otherwise specified
    h. MPN, unclassifiable (MPN-U)
2. A **Myelodysplastic Syndrome (MDS)** is a disorder characterized by abnormalities of the bone marrow, leading to low numbers of one or more types of blood cells. The WHO system recognizes 6 main types of MDS:
    a. MDS with multilineage dysplasia (MDS-MLD)
    b. MDS with single lineage dysplasia (MDS-SLD)
    c. MDS with ring sideroblasts (MDS-RS)

d. MDS with excess blasts (MDS-EB)

e. MDS with isolated del(5q)

f. MDS, unclassifiable (MDS-U)

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Note: The Health Plan uses the genetic testing clinical criteria developed by Concert Genetics, an industry-leader in genetic testing technology assessment and policy development.

Original Effective Date:	07/01/2025
Re-Review Date(s):	June 18, 2025 - Concert Genetics Effective Date: July 01, 2025 (V.2.2025)
	12/16/2025 - Concert Genetics Effective Date: January 01, 2026 (V.1.2026)
Administrative Update:	