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.

RATIONALE AND REFERENCES

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

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)