WHO[1] AND INTERNATIONAL CONSENSUS CLASSIFICATION (ICC)[2] DIAGNOSTIC CRITERIA FOR PRIMARY MYELOFIBROSIS

PMF, prefibrotic stage (pre-PMF)	PMF, fibrotic stage
Major criteria **1. Megakaryocytic proliferation and atypia, without reticulin fibrosis grade >1,[a] accompanied by increased age-adjusted bone marrow cellularity, granulocytic proliferation, and (often) decreased erythropoiesis** **2. Not meeting diagnostic criteria for chronic myeloid leukemia, polycythemia vera, essential thrombocythemia, myelodysplastic neoplasms, or other defined myeloid neoplasms** **3. *JAK2*, *CALR*, or *MPL* mutation or presence of another clonal marker[b] or absence of reactive bone marrow fibrosis[c]**	**Major criteria** **1. Megakaryocytic proliferation and atypia, accompanied by reticulin and/or collagen fibrosis grade 2 or 3[a]** **2. Not meeting diagnostic criteria for chronic myeloid leukemia, polycythemia vera, essential thrombocythemia, myelodysplastic neoplasms, or other defined myeloid neoplasms[d]** **3. *JAK2*, *CALR*, or *MPL* mutation or presence of another clonal marker[e] or absence of reactive bone marrow myelofibrosis[f]**
Minor criteria **• Anemia not attributed to a comorbid condition** **• Leukocytosis ≥11 x 10^9/L** **• Splenomegaly detected clinically and/or by imaging** **• LDH level above the upper limit of the institutional reference range**	**Minor criteria** **• Anemia not attributed to a comorbid condition** **• Leukocytosis ≥11 x 10^9/L** **• Splenomegaly detected clinically and/or by imaging** **• LDH level above the upper limit of the institutional reference range** **• Leukoerythroblastosis**
The diagnosis of prefibrotic-PMF or overt PMF requires all 3 major criteria and at least 1 minor criterion confirmed in 2 consecutive determinations	**The diagnosis of overt primary myelofibrosis requires all 3 major criteria and at least 1 minor criterion to be met in 2 consecutive determinations.**

[a] See MPN-A 2 of 2 for the WHO grading system for myelofibrosis.

[b] In the absence of any of the three major clonal mutations, a search for other mutations associated with myeloid neoplasms (eg, *ASXL1, EZH2, TET2, IDH1, IDH2, SRSF2*, and *SF3B1* mutations) may be of help in determining the clonal nature of the disease.

[c] Minor (grade 1) reticulin fibrosis secondary to infection, autoimmune disorder or other chronic inflammatory conditions, hairy cell leukemia or another lymphoid neoplasm, metastatic malignancy, or toxic (chronic) myelopathies.

[d] Myeloproliferative neoplasms (MPNs) can be associated with monocytosis, or patients can develop it during the course of the disease. These cases may mimic chronic myelomonocytic leukemia; in these rare instances, a history of MPN excludes chronic myelomonocytic leukemia, whereas the presence of MPN features in the bone marrow and/or MPN-associated mutations (in *JAK2, CALR*, or *MPL*) tends to support the diagnosis of MPN with monocytosis rather than chronic myelomonocytic leukemia.

[e] In the absence of any of the three major clonal mutations, a search for other mutations associated with myeloid neoplasms (eg, *ASXL1, EZH2, TET2, IDH1, IDH2, SRSF2,* and *SF3B1* mutations) may be of help in determining the clonal nature of the disease.

[f] Bone marrow fibrosis secondary to infection, autoimmune disorder or another chronic inflammatory condition, hairy cell leukemia or another lymphoid neoplasm, metastatic malignancy, or toxic (chronic) myelopathy.

[1] Adapted with permission from Kanagal-Shamanna R, Naresh KN, Dave SS, et al. Primary myelofibrosis. In: WHO Classification of Tumours Editorial Board. Haematolymphoid tumours [Internet]. Lyon (France): International Agency for Research on Cancer; 2024 [cited 2024 November 15]. (WHO classification of tumours series, 5th ed; vol. 11). Available from: https://tumourclassification.iarc.who.int/chapters/63.

[2] Arber DA, Orazi A, Hasserjian RP, et al. International Consensus Classification of myeloid neoplasms and acute leukemias: Integrating morphologic, clinical and genomic data. Blood 2022;140:1200-1228. from Arber DA, et al. Blood 2022;140:1200-1228.

Note: All recommendations are category 2A unless otherwise indicated.