Oncology Clinical Pathways
Myelodysplastic Syndromes (MDS)

April 2025 – V2.2025

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Myelodysplastic Syndromes – Presumptive Conditions

VA automatically presumes that certain disabilities were caused by military service. This is because of the unique circumstances of a specific Veteran's military service. If a presumed condition is diagnosed in a Veteran within a certain group, they can be awarded disability compensation.

Gulf War and Post 9/11 Veterans

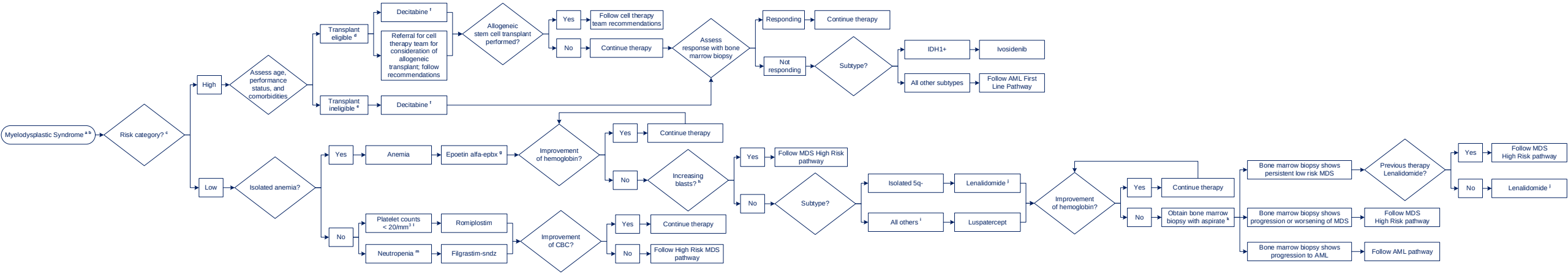
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if the patient served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- Myelodysplastic Syndromes

*The Southwest Asia theater of operations refers to Iraq, Kuwait, Saudi Arabia, the neutral zone between Iraq and Saudi Arabia, Bahrain, Qatar, the United Arab Emirates, Oman, the Gulf of Aden, the Gulf of Oman, the Persian Gulf, the Arabian Sea, the Red Sea, and the airspace above these locations.

For more information, please visit U.S. Department of Veterans Affairs - Presumptive Disability Benefits (va.gov); VA makes several cancers presumptive for service connection Jan 08 2025; eCFR :: 38 CFR 3.320b -- Presumptive service connection for leukemias, multiple myelomas, myelodysplastic syndromes, and myelofibrosis.

Myelodysplastic Syndromes



Clinical trial(s) always considered on pathway. For assistance finding a clinical trial, email CancerClinicalTrialsNavigation@va.gov

[a] **Diagnosis** confirm with blood smear with differential, bone marrow biopsy with aspirate smear, core and clot section, NGS testing, flow cytometry, and karyotype testing; MDS FISH panel if karyotype is suboptimal; NGS includes ASXL1, CBL, DNMT3A, ETV6, EZH2, FLT3, IDH2, KMT2A (MLL), KRAS, NPM1, NRAS, RUNX1, SF3B1, SRSF2, TP53, U2AF1

[b] **Supportive Care and Pre-Therapy Considerations** continue transfusion support during therapy; irradiated units are recommended for patients who are transplant candidates; anti-infectious prophylaxis: VZV/HSV; consider antifungals and antibiotics if there is prolonged neutropenia and recurrent infections, and for patients undergoing treatment; provide vaccinations such as influenza, COVID, and pneumococcal

[c] **Risk Category** low risk includes IPSS-R very low, low, and intermediate without TP53 risk groups; high risk includes IPSS-R intermediate with TP53, high, and very high risk groups; IPSS-M may also be used to categorize risk in MDS

[d] **Transplant Eligible** defined as age <75 years, ECOG PS 0-1, fewer/compensated comorbidities

[e] **Transplant Ineligible** defined as age ≥ 75 years, ECOG PS ≥2, more/uncompensated comorbidities

[f] **Decitabine** response to HMA therapy may require 4-6 cycles of therapy; continue therapy for at least 4-6 cycles to permit response, then perform a repeat bone marrow biopsy and aspirate to assess response; intensity, dose, or frequency may need to be modified based on monitoring

[g] **ESA** recommendation to check erythropoietin (EPO) level prior to initiation of ESA; EPO level >500 IU/L and multiple prior transfusions are associated with lower response rate to ESA therapy; titration of ESA over several months may be needed to ensure adequate exposure and optimal dose when assessing response to ESA; target hemoglobin 10 grams per deciliter; evaluate thrombotic risk

[h] **Blasts** reassess risk stratification; bone marrow biopsy helpful

[i] **SF3B1 Mutation** is associated with superior responses to luspatercept compared to other subtypes

[j] **Lenalidomide** therapy should be continued for at least 2-3 months prior to determination of response; thromboprophylaxis is required

[k] **Bone Marrow Biopsy with Aspirate** consider repeat NGS panel on bone marrow biopsy if there is concern for progression or transformation

[l] **Platelet Counts** treatment to be considered if thrombocytopenia attributable mainly to MDS with clinically significant bleeding or platelets 1) ≤ 20/mm^3 or 2) ≤ 50/mm^3 with a history of bleeding; notably tpo mimetics are associated with secondary bone marrow fibrosis; usually this resolves with drug cessation

[m] **Neutropenia** treatment to be considered if neutropenia attributable mainly to the MDS with clinical manifestation of increased infections or ANC <500/mm^3

CBC Complete Blood Count
ESA Erythropoietin Stimulating Agent
MDS Myelodysplastic Syndrome

Myelodysplastic Syndromes – Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Clinical Suspicion for Myelodysplastic Syndrome (MDS)	Flow Cytometry	Leukemia/lymphoma panel on bone marrow	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	FISH	FISH (-bone marrow or peripheral blood) -- only if karyotype unsatisfactory or logistically difficult to order* MDS panel, including -5/5q; -7/7q; +8; del(20q)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	Karyotyping	Bone marrow karyotype	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
Bone Marrow Morphology Consistent with or Highly Suspicious for Myelodysplastic Syndrome	Somatic NGS**	Targeted myeloid NGS panel required genes include: TP53, KMT2A, FLT3, SF3B1, NPM1, RUNX1, NRAS, ETV6, IDH2, CBL, EZH2, U2AF1, SRSF2, DNMT3A, ASXL1, KRAS; desired but optional genes include: BCOR, BCORL1, CEBPA, ETNK1, GATA2, GNB1, IDH1, NF1, PHF6, PPM1D, PRPF8, PTPN11, SETBP1, STAG2, WT1, DDX41.	GLA Foundation Medicine	GLA Grant*** Yes	Bone Marrow Biopsy, Blood

* FISH does NOT add value in MDS workup unless chromosomes/karyotype are suboptimal; thus, ideally a workflow should be established with the local pathology laboratory or referral lab such that FISH is only performed if chromosomes/karyotype has unsatisfactory resolution or <20 metaphases; in addition, FISH and molecular studies may be performed on a subsequent peripheral blood sample if needed; however, it is understood that in certain resource limited areas this type of reflex testing algorithm may not be possible; in those circumstances it may be in the best interest of the patient to order FISH up front in order to avoid excessive delays in diagnosis

** Can be performed on subsequent peripheral blood sample, as long as neutrophils are at least 20% of total WBC

*** Reach out to GLA for information on use of NGS testing under a VA sponsored grant, with no cost to your local facility