Oncology Clinical Pathways
Essential Thrombocytosis

February 2025 – V1.2025

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Essential Thrombocytosis – 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

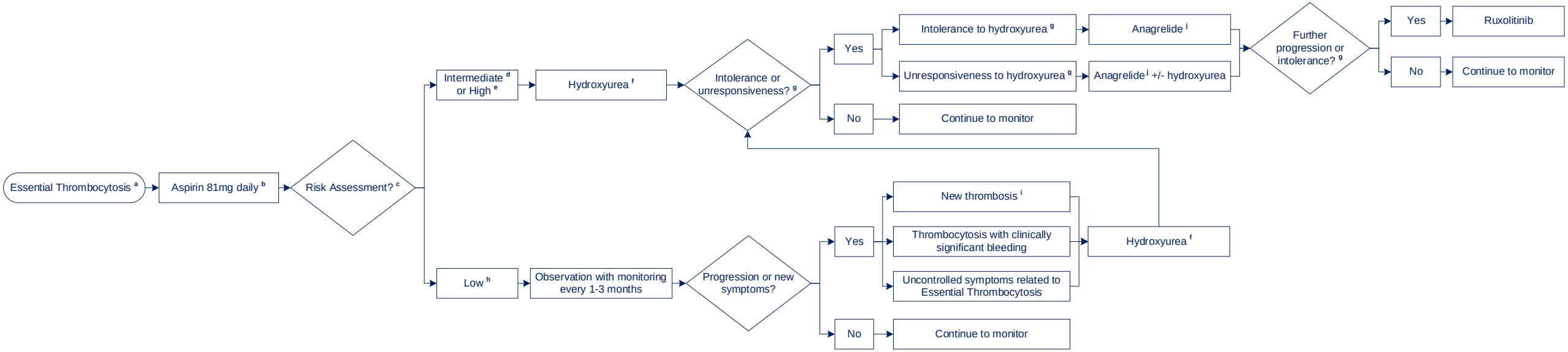
If the patient served on or after Sept. 11, 2001, in Afghanistan, Djibouti, Egypt, Jordan, Lebanon, Syria, Uzbekistan, or Yemen or if the patient served in the *Southwest Asia theater of operations, or Somalia, on or after Aug. 2, 1990, specific conditions include:

- Myelofibrosis

* 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.

Essential Thrombocytosis



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

[a] **Diagnosis** bone marrow biopsy is essential, particularly to identify patients with pre-fibrotic myelofibrosis (this diagnosis tends to have a more aggressive course compared to standard essential thrombocytosis; these patients need to be monitored more closely), reticulin stain for evaluation of fibrosis, JAK2 V617F, MPL, CALR, BCR-ABL1 fusion, and cytogenetics; targeted myeloid NGS panel may be useful for additional prognostication

[b] **Aspirin** is recommended for primary thrombosis prevention in all ET patients without a contraindication; microvascular symptoms can be managed by increasing aspirin to 81mg twice a day; aspirin should follow cytoreductive therapy with hydroxyurea in bleeding associated with ET

[c] **Risk Assessment** includes age > 60, history of thrombosis, cardiovascular risk factors, and JAK2 V617F mutation

[d] **Intermediate Risk** age > 60, no JAK2 mutation, no history of thrombosis, cardiovascular risk

[e] **High Risk** includes any history of thrombosis at any age, or age > 60 years with JAK2 V617F mutation

[f] **Hydroxyurea** start at low doses and titrate up over several weeks with frequent CBC with diff checks; do not increase total weekly dose more than 30-50% to avoid cytopenias; do not adjust dose more than once every two weeks; goal of platelet count reduction should be normalto high-normal range; hydroxyurea should not be given to patients who are pregnant or wishing to become pregnant; pregnancy test is recommended prior to initiation in patients with child-bearing potential; an alternative to hydroxyurea in this patient population is peginterferon alfa-2a

[g] **Intolerance or Unresponsiveness** includes thrombocytosis that is difficult to control and/or significant anemia on hydroxyurea, fevers, rash, ankle ulcers, vasomotor symptoms, worsening splenomegaly, constitutional symptoms; persistent cytopenias should prompt a bone marrow biopsy to assess for myelofibrosis or progression to leukemia; patient compliance should also be assessed

[h] **Low Risk** age ≤ 60, no history of thrombosis, JAK2 V617F mutation

[i] **Treat Thrombosis** as clinically appropriate

[j] **Anagrelide** baseline cardiac evaluation and careful monitoring during treatment recommended; avoid in patients with hypokalemia, with long QT syndrome or concomitant therapies known to prolong QT interval; avoid in pregnancy or those trying to become pregnant; pregnancy test recommended prior to start of therapy

ET Essential Thrombocytosis

Essential Thrombocytosis – Molecular Testing Table

Eligibility	Test Category	Test Type	Recommended Vendors	NPOP Coverage	Specimen Type
Clinical Suspicion of Essential Thrombocythemia (ET)	Stain	Reticulin staining on *bone marrow biopsy	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
	FISH	FISH (Peripheral blood or Bone marrow) to rule out t(9;22) BCR-ABL1	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
	Molecular Testing	MPN reflex test: JAK2 V617F --> CALR (if JAK2 V617F negative) --> MPL (if CALR negative)	Local VA or locally contracted vendor	No	Bone Marrow Biopsy, Blood
Bone Marrow Morphology Consistent with Pre-Fibrotic Primary Myelofibrosis	Somatic NGS **	Targeted myeloid NGS panel including ASXL1, BCOR, BCOR1, CBL, CUX1, DNMT3A, ETV6, EZH2, FLT3, IDH1, IDH2, KRAS, NPM1, NRAS, PHF6, RAD21, RUNX1, SF3B1, SMC1A, SMC3, SRSF2, STAG2, TET2, TP53, U2AF1, ZRSR2, JAK2, CALR, MPL, SETBP1, ETNK1, PTPN11, and NF1. Optional: DDX41.	GLA Foundation Medicine	GLA Grant*** Yes	Bone Marrow Biopsy, Blood
Essential Thrombocythemia (ET) with Myelofibrosis and/or Increased Blasts	Somatic NGS **	Targeted myeloid NGS panel including ASXL1, BCOR, BCOR1, CBL, CUX1, DNMT3A, ETV6, EZH2, FLT3, IDH1, IDH2, KRAS, NPM1, NRAS, PHF6, RAD21, RUNX1, SF3B1, SMC1A, SMC3, SRSF2, STAG2, TET2, TP53, U2AF1, ZRSR2, JAK2, CALR, MPL, SETBP1, ETNK1, PTPN11, and NF1. Optional: DDX41.	GLA Foundation Medicine	GLA Grant*** Yes	Bone Marrow Biopsy, Blood

* For clinically well patients who will only be observed if diagnosis is confirmed, some clinicians prefer to limit workup to peripheral blood and MPN reflex testing only However, bone marrow biopsy is essential to distinguish ET from prefibrotic primary myelofibrosis and is strongly recommended to document baseline fibrosis

** Can be performed on subsequent peripheral blood sample

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