2025

QUICK REFERENCE FOR HEALTHCARE PROVIDERS

MANAGEMENT OF MYELOPROLIFERATIVE NEOPLASMS (SECOND EDITION)

Ministry of Health Malaysia

Malaysian Society of Haematology

Academy of Medicine of Malaysia

KEY MESSAGES

1. Myeloproliferative neoplasms (MPNs) are characterised by clonal expansion of haematopoietic stem cells leading to increased production of one or more blood cells lineages; *BCR::ABL1*-negative MPNs includes essential thrombocythaemia (ET), polycythaemia vera (PV) and primary myelofibrosis (PMF).
2. Diagnostic criteria for MPNs should fulfil the requirement of the World Health Organization (WHO) 2022 classification.
3. Molecular test for *JAK2* V617F should be performed at diagnosis on all patients suspected with MPNs.
4. Risk stratification should be performed upon diagnosis of MPNs subtypes prior to initiation of treatment.
5. Phlebotomy should be considered in patients with PV.
6. In terms of pharmacological treatment in MPNs:
   - Aspirin should be given to all ET and PV patients unless contraindicated.
   - Hydroxyurea (HU) should be used as the first-line treatment; alternatives may include Janus kinase (JAK) inhibitors and interferons (IFNs) in the event of HU intolerance or resistance.
   - Ruxolitinib should be considered in treating intermediate- and high-risk myelofibrosis (MF).
7. Allogeneic haematopoietic stem cell transplant may be considered for intermediate and high-risk MF patients.
8. A multidisciplinary approach should be implemented throughout antenatal care of women with MPNs.
9. Timely referral to haematologists is crucial for optimal management and outcomes for patients with MPN.
10. Monitoring is crucial in managing disease progression, evaluating treatment effectiveness and enhancing outcomes of MPN patients; this is done through a combination of clinical, haematological, molecular and radiological assessments.

This Quick Reference provides key messages & summarises the main recommendations in the Clinical Practice Guidelines (CPG) Management of Myeloproliferative Neoplasms (Second Edition).

Details of the evidence supporting these recommendations can be found in the above CPG, available on the following websites:
Ministry of Health Malaysia: www.moh.gov.my
Academy of Medicine Malaysia: www.acadmed.org.my

CLINICAL PRACTICE GUIDELINES SECRETARIAT
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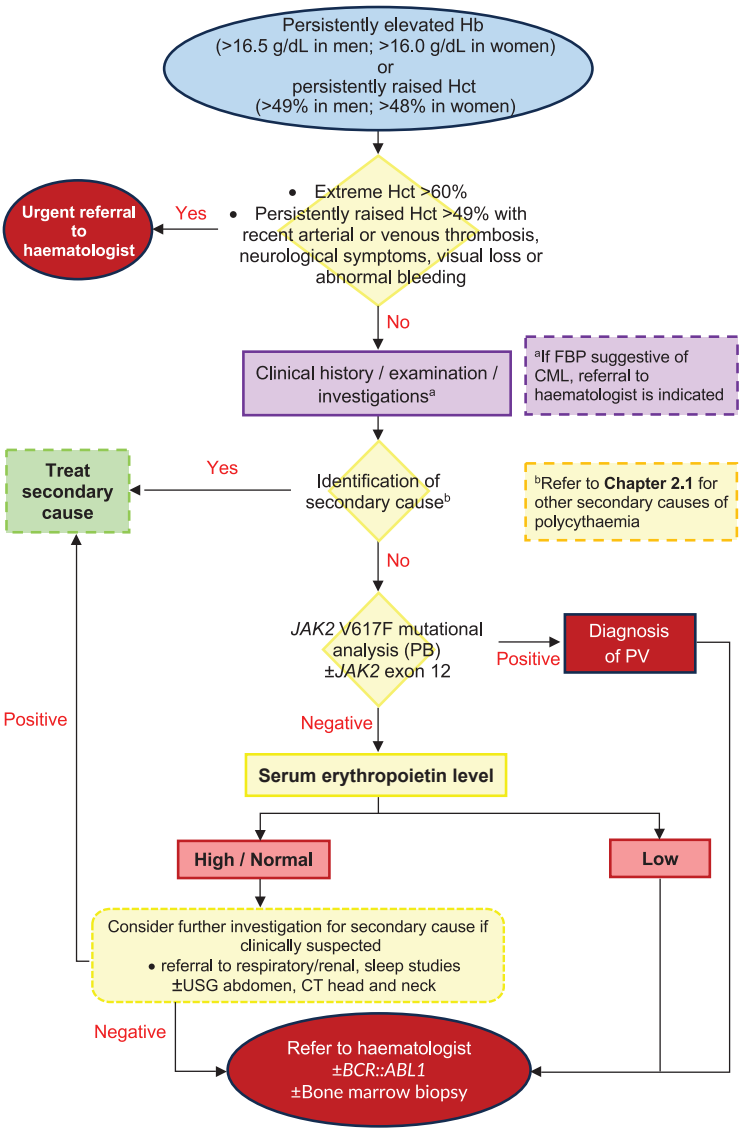
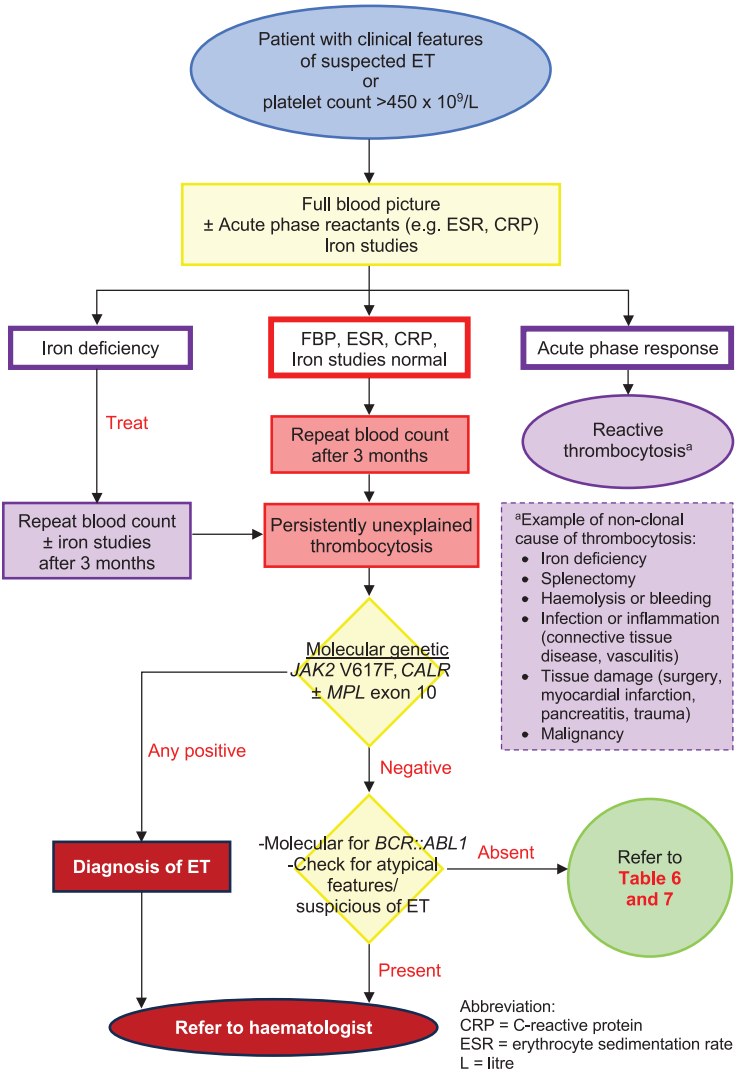
ALGORITHM: DIAGNOSTIC ALGORITHM FOR POLYCYTHAEMIA



Abbreviation:
CML = chronic myeloid leukaemia; CT = computed tomography; g/dL = gram per desilitre; FBP = full blood picture; Hb = haemoglobin; Hct = haematocrit; PB = peripheral blood; USG = ultrasonography

ALGORITHM: DIAGNOSTIC ALGORITHM FOR THROMBOCYTOSIS



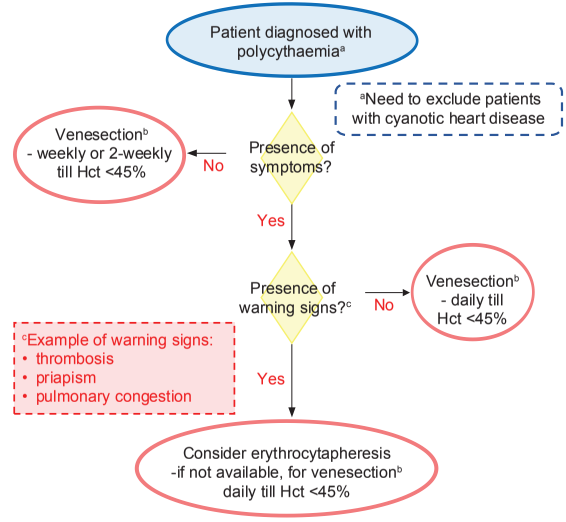
RISK STRATIFICATION

Risk	Attributes	
	PV	ET
Very low		Aged ≤60 years old, negative *JAK2* mutation and no prior thrombosis
Low	Age <60 years old and no prior history of thrombosis	Aged ≤60 years old, positive *JAK2* mutation and no prior thrombosis
Intermediate		Aged >60 years old, negative *JAK2* mutation and no prior thrombosis history
High	Age ≥60 years old or prior history of thrombosis regardless of other factors	Aged >60 years old and positive *JAK2* mutation or prior thrombosis history

PRIMARY MYELOFIBROSIS			
Variables	**IPSS**	**DIPSS**	**DIPSS-plus**
Age >65 years old	1	1	• First determine the risk group based on DIPSS score. • Then score as follows: Low = 0, Intermediate-1 = 1, Intermediate-2 = 2, High = 3. • Lastly, add one point for each of the three additional variables below for final DIPSS-plus score risk group.
Constitutional symptom	1	1	
Hb <10 g/dL	1	2	
Leucocytes >25x10^9/L	1	1	
Circulating blast >1%	1	1	
Platelet count <100x10^9/L			1
RBC transfusion need			1
*Unfavourable karyotype			1

Risk groups	Points	Points	Points
Low	0	0	0
Intermediate-1	1	1 - 2	1
Intermediate-2	2	3 - 4	2 - 3
High	≥3	5 - 6	≥4

ALGORITHM: POLYCYTHAEMIA VENESECTION



KEY POINTS:

- All patients should be on aspirin, caution for patients with acquired von Willebrand syndrome
- [b]Target of venesection: Hct of 45% (equates to Hb of 15 g/dL) in PV
- [b]Blood should be venesected over ≥15 minutes to a maximum of 7 mL/kg, i.e. ≈ 400 mL in <60 kg, ≈ 500 mL in 70 kg, ≈ 650mL in 90 kg using likely lean body weight.

MEDICATION TABLE

Drug	Recommended Dose, Administration and Adjustment	Common Adverse Effects	Pregnancy and Lactation / Precautions / Remarks
Platelet Aggregation Inhibitor / Blood Modifier Agent			
Aspirin Aspirin/Glycine	75 - 100 mg OD PO	Gastric ulcer, Haemorrhage, Exudative age-related macular degeneration	**Pregnancy**: Foetal harm is similar to normal population. There is only low risk of postpartum hemorrhage for low dose aspirin. **Lactation**: Infant risk cannot be ruled out
Platelet reducing agent / Blood Modifier Agent			
Anagrelide	Initial, 0.5 mg BD - QID PO or 1 mg BD PO for at least 1 week; titrate to the lowest effective dose; do not exceed 0.5 mg/day dose increase in any 1 week; maximum 2.5 mg/dose and 10 mg/day	Oedema, Palpitations, Abdominal pain, Diarrhoea, Nausea, Headache, Dizziness, Pain, Asthenia, Dyspnoea	**Pregnancy**: Foetal risk cannot be ruled out, not recommended **Lactation**: Infant risk cannot be ruled out. Breastfeeding is not recommended during and for 1 week after the last dose
Immunomodulators			
Peginterferon Alpha-2a	**Essential Thrombocythemia** Initial, SC 90 mcg/week, modify dose based on efficacy and toxicity **Polycythaemia vera** Initial, SC 90 mcg/week, escalated every 2 weeks to 135 mcg/week (maximum 180 mcg/week)	Alopecia, Pruritus, Abdominal pain, Anorexia, Diarrhoea, Nausea, Vomiting, Neutropenia, Raised liver enzymes, Anxiety, Depression, Dizziness, Fatigue, Headache, Insomnia, Rigors, Arthralgia, Myalgia, Cough, Flu-like symptoms, Fever	**Pregnancy:** Cautious under expert's supervision **Lactation:** Infant risk cannot be ruled out, relatively contraindicated **Contraindications:** • Autoimmune hepatitis • Hepatic decompensation (Child-Pugh class B and C) in cirrhotic before or during treatment • Known hypersensitivity to IFN-alfa or its components
Antineoplastic Agent			
Hydroxyurea	20 - 30 mg/kg OD PO Do not open capsules and avoid exposure to crushed or opened capsules. Take at the same time each day, with a glass of water.	Alopecia, Rash, Nail discolouration, Skin or oral ulcer, Dry skin, Diarrhoea, Nausea, Cytopaenia, Infection, Arthralgia, Backache, Headache, Dizziness, Cough, Dyspnoea, Fatigue, Fever	**Pregnancy**: May cause foetal harm **Lactation**: Advise women not to breastfeed during therapy Live vaccines: increased risk of infection
Tyrosine Kinase Inhibitor (JAK inhibitor)			
Ruxolitinib	**MF, intermediate- or high-risk** Baseline platelet >200 x 10^9/L: 20 mg BD PO Baseline platelet 101 - 200 x 10^9/L: 15 mg BD PO Baseline platelet 50 - 100 x 10^9/L: 5 mg BD PO **Polycythemia vera, intolerant to hydroxyurea:** 10 mg BD PO	Cytopaenias, bruising, dizziness, headache, urinary tract infection, raised liver enzymes, hypercholesterolaemia	**Pregnancy:** Not recommended **Lactation:** Discontinue breastfeeding during treatment until 2 weeks after the final dose

Abbreviation: BD = *bis in die*/ twice daily; mcg = microgram; mg = milligram; OD = *omne in die*/ once daily; PO = *per os*/ orally; QID = *quarter in die*/ four times a day; SC = subcutaneous

TREATMENT FOR PREGNANT WOMEN WITH MPNs

Risk factor	Antenatal	Post-natal
High risk pregnancy		
• Previous history of arterial thrombosis due to PV	• Commence IFN • Prophylactic dose low molecular weight heparin (LMWH) twice daily • Aspirin	• Reduce LMWH to once daily prophylactic dose for 6 weeks • Aspirin • Decision to continue IFN based on individual patient discussion
• Previous history of venous thrombosis due to PV, previous pregnancy complications (>3 first trimester loss, >1 third trimester loss, birth weight <5th centile of gestation, intrauterine death or stillbirth, pre-eclampsia	• Commence IFN • Prophylactic dose LMWH once daily, then consider to increase the dose twice daily from 16 weeks onwards until delivery • Aspirin from confirmation of pregnancy	• Continue once daily prophylactic dose LMWH until 6 weeks • Aspirin • Decision to continue IFN based on individual patient discussion
• Previous history of haemorrhage due to PV or significant antepartum or postpartum haemorrhage requiring transfusion	• Commence IFN • Addition or continuation of aspirin to be decided on patient-specific basis	• Continue aspirin • Once daily prophylactic dose LMWH for 6 weeks • Decision to continue IFN based on individual patient discussion
• Thrombocytosis, platelet count >1500 x 10^9/L before or during pregnancy and/or diabetes mellitus or hypertension requiring pharmacological treatment	• Commence IFN • Continue aspirin	• Continue once daily prophylactic dose LMWH until 6 weeks • Aspirin • Decision to continue IFN based on individual patient discussion
Standard risk pregnancy		
All other pregnancies	• Commence aspirin	• Commence once daily prophylactic dose LMWH for 6 weeks • Aspirin

- All women with MPNs should be given pre-pregnancy counselling prior to conception.
- All pregnant women with MPNs should be prescribed with aspirin unless contraindicated; its combination with low molecular weight heparin and/or interferon is preferred in high-risk patients.

REFERRAL CRITERIA

Type of referral	Polycythaemia	Thrombocytosis	Anaemia
Urgent	• Extreme raised Hct >60% • Persistently raised Hct >49% in association with recent arterial or venous thrombosis, neurological symptoms, visual loss or abnormal bleeding	• Platelet count >1,000 x 10^9/L • Platelet count 600 - 1,000 x 10^9/L in association with recent arterial or venous thrombosis, neurological symptoms or new abnormal bleeding	• Unexplained progressive symptomatic anaemia • Anaemia in association with splenomegaly, lymphadenopathy or other cytopaenias
Non-urgent	• Elevated Hct (male >49%, female >48%) in association with past history of arterial or venous thrombosis, splenomegaly, pruritus, elevated white blood cell (WBC) or platelet counts • Persistent (>3 months) unexplained elevated Hct (male >49%, female >48%)	• Persistent (i.e. lasting >6 months), unexplained thrombocytosis >450 x 10^9/L	• Persistent unexplained anaemia

MONITORING IN PRIMARY CARE SETTINGS

Polycythaemia	Thrombocytosis	Anaemia
• Serial full blood counts (FBC) (non-fasting blood samples with patient in well-hydrated state) • FBP - indicated for Hct >52% (males) or >49% (females) on second presentation • Modify known associated lifestyle factors: smoking, alcohol, diuretics and SGLT2 inhibitors • Screen for diabetes mellitus	• FBP - indicated for persistently elevated platelet count >450 x 10^9/L (for ≥6 months) • Investigate and treat secondary causes: ○ Ferritin and iron studies - iron deficiency ○ Elevated CRP/ESR - reactive thrombocytosis ○ Rule out infection, inflammation or neoplasia	• Detailed history - focus on duration, symptoms, bleeding, diet, drug and family history • FBP and reticulocyte count • FBP - indicated for: ○ first Hb <8.5 g/dL OR ○ Hb <10g/dL if RDW >17% in the presence of reticulocytosis • Ferritin, B12 and folate, serum iron, TIBC, transferrin saturation (this will be more informative than ferritin if there is an inflammatory component) • Serum immunoglobulins and protein electrophoresis • Renal and liver biochemistry • Monitor FBC for evidence of progression over time