Optimal care pathway for people with Myeloproliferative neoplasms (MPN)

Quick reference guide

Support: Assess supportive care needs at every step of the pathway and refer to appropriate health professionals or organisations.

The optimal care pathways describe the standard of care that should be available to all cancer patients treated in Australia. The pathways support patients and carers, health systems, health professionals and services, and encourage consistent optimal treatment and supportive care at each stage of a patient's journey. Seven key principles underpin the guidance provided in the pathways: patient-centred care; safe and quality care; multidisciplinary care; supportive care; care coordination; communication; and research and clinical trials. This quick reference guide provides a summary for clinicians of the *Optimal care pathway for people with Myeloproliferative neoplasms.*

Please note that not all patients will follow every step of the pathway.

Step 1: Prevention and early detection

Prevention

The causative factors of MPNs are not yet known and there is no evidence that MPNs can be prevented.

Risk factors

The known risk factors for developing MPNs are:

- smoking
- genetic risk (relatives of MPN patients have an increased risk of developing an MPN)
- age (occurs mainly in people aged over 60).

Early detection

There is often a long lead up to diagnosis of MPNs. Patients with thrombotic events in unusual sites (e.g., the splanchnic vein and cerebral sinuses) should be screened for MPNs with a full blood count and testing for JAK2 mutation. JAK2 testing should be undertaken regardless of the blood results.

Screening recommendations

Routine screening for MPNs is not currently recommended in the general population.

General health checklist

- ❑ Recent weight changes discussed and the patient's weight recorded
- ❑ Alcohol intake and smoking status discussed and support offered if appropriate
- ❑ Physical activity recorded
- ❑ Referral to a dietitian considered

Step 2: Presentation, initial investigations and referral

While many patients with MPNs are asymptomatic, MPNs can be identified with routine testing and full blood examinations. Symptoms, where present, can include:

- fatigue
- early satiety
- unexplained weight loss
- fever or night sweats
- itching/Pruritus (especially after exposure to water)
- erythromelalgia (burning pain in the hands and feet in response to heat)
- abdominal discomfort
- gout.

In patients with PV or ET other clinical manifestations include headaches, dizziness, visual disturbances and plethora. Venous thromboembolism and thrombosis in unusual sites may also be present in patients with ET.

Additional symptoms common to myelofibrosis (aside from those listed above) include extramedullary haematopoiesis and hepatosplenomegaly.

If the following blood test abnormalities are found, an MPN should be investigated as a possible underlying cause: polycythaemia, leucocytosis, thrombocytosis, low blood count, left shift or increase in immature white cell precursors.

Initial investigations by the GP should include:

- full blood examination
- selective investigations (as clinically appropriate) to exclude secondary causes
- molecular testing for driver mutations (either JAK2, CALR or MPL depending on what is suspected)
- lactate dehydrogenase (LDH) and urate.

Checklist

- ❑ Polycythaemia, leucocytosis, thrombocytosis, low blood count, left shift or increase in immature white cell precursors
- ❑ Signs and symptoms recorded
- ❑ Patient notified of support services such as Cancer Council 13 11 20, Leukaemia Foundation 1800 620 420
- ❑ Referral options discussed with the patient and/or carer including cost implications

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Step 2: Presentation, initial investigations and referral continued

Referral options

At the referral stage, the patient's GP or other referring doctor should advise the patient about their options for referral, waiting periods, expertise, potential out-of-pocket costs and the range of services available. This will enable patients to make an informed choice of specialist and health service.

Communication

The GP's responsibilities include:

- explaining to the patient and/or carer who they are being referred to and why
- supporting the patient and/or carer while waiting for specialist appointments
- informing the patient and/or carer that they can contact Cancer Council 13 11 20 and Leukaemia Foundation 1800 620 420.

Timeframe

If the patient is asymptomatic, repeat testing should be performed **within 8 weeks**. If there are persistent raised blood counts without a clear cause, splenomegaly and / or anaemia with constitutional symptoms it is recommended that GPs refer patients **within 8 weeks**.

Cases that require prompt referral to a specialist **within 1 week** are: a patient that is symptomatic, a critically abnormal blood count and / or evidence of unexplained arterial or unusual site venous thrombosis. Performing genetic testing for driver mutations while awaiting haematology may assist in expediting the diagnosis.

Step 3: Diagnosis, staging and treatment planning

The initial workup for patients with a suspected MPN should include:

- full blood examination and film
- chest x-ray
- abdominal ultrasound scan
- bone marrow aspiration and trephine biopsy with samples sent for cytogenetics
- bone marrow testing to confirm the diagnosis, asses marrow morphology and degree of reticulin fibrosis
- review and optimisation of cardiovascular risk factors
- screen for acquired Von Willebrand Disease
- molecular testing performed by a specialist haematologist experienced in the care of MPN.

Genetic testing

If not carried out by the referring practitioner, genetic testing should be undertaken. In cases of clinically suspected PV, a test for JAK2 (or panel including JAK2 exon 12 if JAK2 V617F is negative) should always be included. For all other MPNs, the diagnostic approach should include screens for JAK2, CALR and MPL. Demonstration of a clonal marker is not a requirement for diagnosis of primary myelofibrosis if reactive causes can be excluded.

Treatment planning

The multidisciplinary team should discuss patients with MPN before starting any disease-directed therapy.

Research and clinical trials

Consider enrolment where available and appropriate. See the OCP resources appendix and relevant steps for clinical trial resources relevant to MPN.

Communication

The lead clinician's[1] responsibilities include:

- discussing a timeframe for diagnosis and treatment options with the patient and/or carer
- explaining the role of the multidisciplinary team in treatment planning and ongoing care
- encouraging discussion about the diagnosis, prognosis, advance care planning and palliative care while clarifying the patient's wishes, needs, beliefs and expectations, and their ability to comprehend the communication

Checklist

- ❑ Diagnosis has been confirmed
- ❑ Performance status and comorbidities measured and recorded
- ❑ Patient discussed at multidisciplinary meetings and decisions provided to the patient and/or carer
- ❑ Clinical trial considered
- ❑ Supportive care needs assessed and referrals to allied health services actioned as required
- ❑ Referral to support services (such as Cancer Council, Leukaemia Foundation, Lymphoma Australia)
- ❑ Treatment costs discussed with the patient and/or carer

1 Lead clinician – the clinician who is responsible for managing patient care.
The lead clinician may change over time depending on the stage of the care pathway and where care is being provided.

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Step 3: Diagnosis, staging and treatment planning continued

- providing appropriate information and referral to support services as required
- communicating with the patient's GP about the diagnosis, treatment plan and recommendations from multidisciplinary meetings.

Timeframe

Baseline investigations should be completed **within 3 months** for routine cases.

Step 4: Treatment

Establish intent of treatment

- curative
- anti-cancer therapy to improve quality of life and/or longevity without expectation of cure
- symptom palliation.

Systemic therapy

Allogeneic stem cell transplant is currently the only curative therapy but is reserved for high-risk patients.

Treatment of PV and ET

Cytoreductive therapy (Hydroxyurea, pegylated interferon or pegylated interferon alfa-2a depending on the patient) should be considered for high-risk patients with PV or ET and those with progressive splenomegaly, leucocytosis, thrombocytosis, persistently elevated counts despite venesection or poor tolerance of venesection.

For patients with PV, phlebotomy should be used to maintain a haematocrit <45% and low dose aspirin should be given to all patients who do not have any contraindications.

Treatment of MF

Treatment principles for MF apply equally to PMF, post PV-MF and post-EF-MF. Management of PMF is dependent on the risk score of the disease. Ruxolitinib is the standard of care for eligible patients.

The management of prefibrotic MF includes the management of symptom burden and cytoreduction to control thrombocytosis or leucocytosis. For young patients with low-risk disease and minimal symptomatology, a watch and wait approach may be used in conjunction with antiplatelet agents.

Supportive therapies

A priority for the treatment of MPNs is optimising symptom management and quality of life through supportive therapies. This should include:

- antiplatelet therapy for all JAK2 mutated MPN (including PV), and MPL mutant ET and MF to prevent index and recurrent thrombotic complications. Aspirin is the preferred agent but if contraindicated, clopidogrel is acceptable
- for patients with predominant anaemia, treatment with androgens, prednisone (PBS funded therapy), thalidomide, lenalidomide or danazol is recommended
- assessment of cardiovascular risk factors at baseline and annually using a validated score (e.g., the QRISK score).

Radiation therapy

This modality has generally been surpassed by other emerging therapies. It should only be considered for early-stage MF with refractory hypersplenism following a multidisciplinary team meeting.

Palliative care

Early referral to palliative care can improve quality of life and in some cases survival. Referral should be based on need, not prognosis. For more information, visit the Palliative Care Australia website <www.palliativecare.org.au>.

Communication

The lead clinician and team's responsibilities include:

- discussing treatment options with the patient and/or carer including the intent of treatment as well as risks and benefits
- discussing advance care planning with the patient and/or carer where appropriate
- communicating the treatment plan to the patient's GP
- helping patients to find appropriate support for exercise programs where appropriate to improve treatment outcomes.

Checklist

- ❑ Intent, risk and benefits of treatment discussed with the patient and/or carer
- ❑ Treatment plan discussed with the patient and/or carer and provided to GP
- ❑ Supportive care needs assessed and referrals to allied health services actioned as required
- ❑ Early referral to palliative care considered and advance care planning discussed with the patient and/or carer

Timeframe

Cytoreductive/antiplatelet/anticoagulant therapy should be **initiated immediately** in patients with thrombotic complications. Treatment timeframes in other MPNs are dependent on the prognostic and thrombotic risk of the patient. Due to the long survival in many patients with MPN it may be prudent to delay cytoreductive therapy until signs of high-risk disease.

Radiation therapy is only used as a last resort and should be delayed until other therapies have failed.

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Step 5: Care after initial treatment and recovery

Provide a treatment and follow-up summary to the patient, carer and GP outlining:

- the diagnosis, including tests performed and results
- treatment received (types and date)
- current toxicities (severity, management and expected outcomes)
- interventions and treatment plans from other health professionals
- potential long-term and late effects of treatment and care of these
- supportive care services provided
- a follow-up schedule, including tests required and timing
- contact information for key healthcare providers who can offer support for lifestyle modification
- a process for rapid re-entry to medical services for any issues arising.

Communication

The lead clinician's responsibilities include:

- explaining the treatment summary and follow-up care plan to the patient and/or carer
- informing the patient and/or carer about secondary prevention and healthy living
- discussing the follow-up care plan with the patient's GP.

Checklist

- ❑ Treatment and follow-up summary provided to the patient and/or carer and the patient's GP
- ❑ Supportive care needs assessed and referrals to allied health services actioned as required
- ❑ Patient-reported outcome measures recorded

Step 6: Managing relapsed or progressive disease

Detection

Most progressive disease will be detected via routine follow-up or by the patient presenting with symptoms.

Treatment

Evaluate each patient for whether referral to the original multidisciplinary team is appropriate. Treatment will depend on the features of disease, previous management and the patient's preferences.

Advance care planning

Advance care planning is important for all patients but especially those with advanced disease. It allows them to plan for their future health and personal care by thinking about their values and preferences. This can guide future treatment if the patient is unable to speak for themselves.

Survivorship and palliative care

Survivorship and palliative care should be addressed and offered early. Early referral to palliative care can improve quality of life. Referral should be based on need, not prognosis.

Communication

The lead clinician and team's responsibilities include:

- explaining the treatment intent, likely outcomes and side effects to the patient and/or carer and the patient's GP.

Checklist

- ❑ Treatment intent, likely outcomes and side effects explained to the patient and/or carer and the patient's GP
- ❑ Supportive care needs assessed and referrals to allied health services actioned as required
- ❑ Advance care planning discussed with the patient and/or carer
- ❑ Patient referred to palliative care if appropriate
- ❑ Routine follow-up visits scheduled

Step 7: End-of-life care

Palliative care

Consider a referral to palliative care. Ensure an advance care directive is in place.

Communication

The lead clinician's responsibilities include:

- being open about the prognosis and discussing palliative care options with the patient
- establishing transition plans to ensure the patient's needs and goals are considered in the appropriate environment.

Checklist

- ❑ Supportive care needs assessed and referrals to allied health services actioned as required
- ❑ Patient referred to palliative care
- ❑ Advance care directive in place

Visit our guides to best cancer care webpage <www.cancercareguides.org.au> for consumer guides. Visit our OCP webpage <www.cancer.org.au/OCP> for the optimal care pathway and instructions on how to import these guides into your GP software.

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