Optimal care pathway for people with low-grade lymphomas

Quick reference guide

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 low-grade lymphomas.*

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

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

Step 1: Prevention and early detection

The optimal care pathway for low-grade lymphomas (LGLs) covers follicular lymphoma (FL), marginal zone lymphoma (MZL) and mantle cell lymphoma (MCL).

Prevention

The causes of most LGLs are not fully understood and there are currently no clear prevention strategies. Some LGLs such as gastric mucosa-associated lymphoid tissue (MALT) lymphoma are, however, preventable through identifying and eradicating a *Helicobacter pylori* infection.

Risk factors

Risk factors in common across all LGLs are:

- advanced age and family history of LGL
- obesity
- prior radiation or chemotherapy
- weakened immune system
- autoimmune disease
- exposure to glyphosate-based agricultural pesticides (a possible risk).

Specific risk factors for MZL include:

- *Helicobacter pylori* gastritis – in gastric MALT lymphomas
- splenic MZL (SMZL), in people with chronic hepatitis C infection.

Specific risk factors for MCL include:

- gender – males have a greater risk.

Early detection

There is no established role for screening for LGLs. People at risk of developing lymphomas related to immunodeficiency should be told of this increased risk.

General health checklist

- ❑ Recent weight changes discussed and recorded
- ❑ Alcohol intake and smoking status discussed and support offered if appropriate
- ❑ Physical activity recorded
- ❑ Referral to a dietitian, physiotherapist or exercise physiologist considered
- ❑ Sun smart advice

Step 2: Presentation, initial investigations and referral

LGLs frequently present with symptoms of gradual onset occurring over weeks or months. People can be asymptomatic at diagnosis, with LGL discovered incidentally after imaging or laboratory tests reveal an abnormality.

The following signs and symptoms should be investigated:

- a lump or mass in any organ
- lymphadenopathy, particularly lymphadenopathy lasting more than 2 weeks
- splenomegaly
- one or more of these systemic symptoms even in the absence of lymphadenopathy: fever, drenching night sweats, unexplained weight loss, frequent infections
- unexplained cytopenias
- persistent lymphocytosis.

Indicators of concern that should lead to prompt referral to a specialist include:

- symptoms or results indicating organ dysfunction and low blood counts
- markedly elevated LDH
- marked B symptoms (weight loss > 10%, persistent fevers > 38°C, or persistent drenching night sweats).

Checklist

- ❑ Signs and symptoms recorded
- ❑ Supportive care needs assessed and referrals to allied health services actioned as required
- ❑ Patient notified of support services such as Cancer Council 13 11 20, Leukaemia Foundation 1800 620 420 and Lymphoma Australia 1800 953 081
- ❑ Referral options discussed with the patient and/or carer including cost implications

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

Step 2: Presentation, initial investigations and referral continued

Initial investigations by a GP include:

Where there are no indicators of concern (listed above), perform these investigations:

- blood tests to assess organ dysfunction, but no laboratory test can exclude these lymphomas
- imaging of the affected area including ultrasound, chest radiography and CT scan as appropriate
- biopsy or direct specialist referral as appropriate.

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, Leukaemia Foundation and Lymphoma Australia.

Timeframe

For patients with indicators of concern, urgent referral to a specialist centre and rapid access to specialist evaluation and review is needed. Where lymphoma is proven by biopsy, or strongly suspected, referral to specialist should occur **within 72 hours**.

Where there are no indicators of concern, initial investigations should take place and referral to a specialist should occur **within 4 weeks**.

Step 3: Diagnosis, staging and treatment planning

Diagnosis

A tissue diagnosis is required before initiating definitive treatment, although one may have been performed before referral. Fresh and fixed tissue samples should be collected from the tissue biopsy for anatomical pathology and flow cytometry. Gene mutation testing may be of prognostic relevance in some cases.

Evaluate relevant organ function based on history, clinical examination and, where appropriate, laboratory or imaging investigations (cardiac, respiratory, renal, hepatic).

Staging and prognosis

Disease stage should be confirmed with an FDG-PET/CT scan and may include bone marrow evaluation. Other tests may be performed to evaluate the prognosis.

Genetic testing

Currently there are no genetic tests applicable to predict family risk of LGL.

Treatment planning

The multidisciplinary team should discuss all newly diagnosed patients with LGL prior to commencing any disease-directed therapy.

Research and clinical trials

See the OCP resources appendix and relevant steps for clinical trial resources relevant to LGL.

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
- 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
- explaining the principles of 'watchful waiting' if active surveillance is planned rather than commencing treatment.

Checklist

- ❑ Diagnosis has been confirmed
- ❑ Full histology obtained
- ❑ Performance status and comorbidities recorded
- ❑ Patient discussed at multidisciplinary meeting and decisions provided to the patient and/or carer
- ❑ Clinical trials 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

Timeframe

Referrals should be triaged on the basis of presence of indicators of concern and the timing of diagnostic investigations should be guided by the initial severity of symptoms. Staging should be completed **within 4 weeks**.

All cases should be reviewed at a multidisciplinary meeting.

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.

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

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

Watchful waiting (WW) is appropriate for asymptomatic FL and MZL in stage II (which is not suited to radiotherapy) and advanced-stage FL and MZL (stages III and IV). The frequency of clinical review is based on the tempo of the disease, the comfort of the patient with a WW approach and the likelihood that they will recognise and re-present at signs of relapse. WW can cause significant psychological distress, so referral to a psycho-oncology service experienced in lymphoma is recommended.

Indolent MCL, commonly a leukaemic presentation, indicated by lack of symptoms and low tumour burden, can be followed with WW.

Infection eradication of *Helicobacter pylori* may induce remission for gastric MALT without the need for radiotherapy.

Radiation therapy has an important role in specific scenarios within indolent lymphoma subtypes:

- potentially curable for early-stage FL (stage I and stage II in which lymph nodes are contiguous)
- potentially curable for early-stage MZL (including gastric, cutaneous, unilateral and bilateral orbital MALT, and other localised MZLs)
- used for symptom control in advanced-stage LGL, where lymphoma is impairing quality of life.

Systemic therapy is appropriate in most patients with FL and MZL with non-contiguous stage II or stage III–IV disease who are symptomatic. Systemic therapy is most commonly used with chemotherapy and anti-CD20 monoclonal antibody. MCL causing symptoms should be treated with systemic chemotherapy and anti-CD20 monoclonal antibody combination, incorporating high-dose cytarabine in younger, fitter patients, followed by consolidation with autologous stem cell transplantation.

Surgery is a potential first-line treatment option (splenectomy) for splenic MZL.

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

Treatment may start after a long WW period; however, where there are symptoms of concern treatment should start urgently.

In FL and MZL, the decision of when to start systemic therapy is guided by the internationally accepted standard criteria and treatment should begin **within 4 weeks**.

Most symptomatic MCL patients should begin treatment with systemic therapy **within 2 weeks** of completing staging.

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

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
- tumour characteristics
- treatment received (types and date)
- current toxicities
- 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 suspected recurrence.

Communication

The lead clinician's responsibilities include:

- explaining the treatment summary and follow-up care plan to the patient and/or carer
- 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 refractory, relapsed, residual or progressive disease

Detection

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

Re-biopsy is strongly encouraged to confirm relapse and to clarify the nature of the relapsed lymphoma.

Treatment

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

Watchful waiting active surveillance of relapse rather than immediate treatment is commonly recommended.

Systemic therapy options depend on the duration of response to first-line therapy and include: chemotherapy with anti-CD20 monoclonal antibody with or without autologous transplantation, novel targeted treatments and enrolment onto a clinical trial.

Radiotherapy may be appropriate to treat localised relapse.

Advance care planning

Advance care planning is important for all patients but especially those with relapsed 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 and in some cases survival. 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 the guides to best cancer care webpage <www.cancercareguides.org.au> for consumer guides. Visit the OCP webpage <www.cancer.org.au/OCP> for the optimal care pathway and instructions on how to import these guides into your GP software.

Endorsed by:

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