

Optimal care pathway for people with chronic lymphocytic leukaemia

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 of the *Optimal care pathway for people with chronic lymphocytic leukaemia* (CLL).

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

Step 1: Prevention and early detection

Prevention

The cause of CLL is unknown and there are currently no effective prevention strategies. At present, there is no evidence linking lifestyle or behavioural factors to prevention of CLL.

Risk factors

The risk factors for developing CLL include the following:

- age (occurs mainly in people aged over 60)
- gender (CLL is more common in males)
- having a first-degree relative with CLL or other lymphoproliferative disorder
- Caucasians are more likely to get CLL

- exposure to chemicals such as Agent Orange is linked to lymphoproliferative disorders generally. Any potential causative link to CLL specifically has not been definitively established.

Early detection

CLL is usually slow growing and, in most cases, it is picked up early during routine blood tests for unrelated conditions. There is currently no established benefit from early detection.

Screening recommendations

Routine screening for CLL is not currently recommended in either the general population or in relatives of people with CLL.

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

Most patients are asymptomatic when they are diagnosed because CLL is often found in routine blood tests.

When present, symptoms can include:

- painless swelling of lymph nodes (often around the neck) that may fluctuate in size but don't completely resolve (within 6 weeks)
- unexplained weight loss of ≥ 10 per cent of body weight within the past 6 months
- fever or severe night sweats without signs of infection (uncommon)
- extreme fatigue frequent infections or first onset of herpes zoster reactivation.

Other signs may include enlarged lymph nodes, spleen or liver, with enlarged lymph nodes being the most common of these.

Additionally, if the following blood test abnormalities are found, CLL should be investigated as a possible underlying cause: reduced levels of normal immunoglobulins, autoimmune haemolytic anaemia, immune thrombocytopenia.

Initial investigations by the GP include:

- history and physical exam including careful palpation of all lymph node areas, spleen and liver
- full blood count and manual film examination
- flow cytometry to confirm clonal nature of lymphocytes
- urea, electrolytes, uric acid and creatinine
- liver function tests
- serum immunoglobulin levels and direct antiglobulin test (Coombs test).

Checklist

- Significant lymphocytosis and/or a leukaemic cell population is identified
- Signs and symptoms recorded
- 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

Step 2: Presentation, initial investigations and referral continued

Lymph node biopsy is generally not necessary to diagnose CLL, even if lymphadenopathy is present clinically or on imaging. Routine imaging is not recommended and should only be performed when there are concerns about local symptoms, compression or very bulky nodes to exclude a local complication such as hydronephrosis or vascular compression.

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, Leukaemia Foundation 1800 620 420 and Lymphoma Australia 1800 953 081.

Timeframe

The timeframe to begin investigations is rarely urgent. For patients with severe symptoms of fever, night sweats or weight loss, investigations should be started **as soon as possible** to exclude more aggressive disorders such as lymphoma. Patients should generally be seen by a specialist **within 2 weeks** of GP referral. However, if severe thrombocytopenia, anaemia or bulky or locally compressive lymphadenopathy is present, refer **within 72 hours**.

Step 3: Diagnosis, staging and treatment planning

Diagnosis for CLL will be confirmed based on full blood count and a thorough physical examination, including all lymph node areas, spleen and liver.

Investigations for baseline assessment and to inform prognosis include: detailed blood chemistry tests, chest radiograph and viral serology.

The following investigations are only recommended under certain circumstances:

- marrow aspirate and biopsy when the cause of low blood counts is unclear, disease phenotype is inconclusive, or the exact diagnosis is uncertain
- CT scans PET scan, MRI or ultrasound are not recommended for asymptomatic patients or during routine evaluation. Exceptions include: PET scans for patients with confirmed or suspected Richter's syndrome or imaging of bulky or painful lymphadenopathy or significant symptoms or physical findings that suggest a local compressive complication

- for patients who do have symptoms, or where treatment will be initiated, CT scans are necessary to assess the tumour burden and risk of tumour lysis syndrome.

Molecular genetic testing

The following tests are not recommended at diagnosis but should be done before starting treatment or when there are signs of disease progression that may soon lead to treatment:

- interphase FISH for del(13q), del(11q), del(17p), +12 and DNA sequencing for the presence of a TP53 mutation
- IGHV mutational status.

Treatment planning

The multidisciplinary team should discuss patients with CLL 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 CLL.

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

Step 3: Diagnosis, staging and treatment planning continued

Communication

The lead clinician's¹ 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.

Timeframe

Baseline investigations should be performed **2–4 weeks before** starting treatment, CT scans can be done **up to 2 months prior**. Molecular cytogenetics (FISH), marrow aspirate and biopsy can be performed **up to 12 months before** starting treatment, provided that there have been no intervening therapies and the general disease course is unchanged.

Step 4: Treatment

Treating asymptomatic early-stage CLL does not improve survival, so an initial 'watch and wait' approach is recommended. Disease-directed therapy should not start unless there are disease-related symptoms or evidence of disease progression.

Establish intent of treatment

- Curative
- Anti-cancer therapy to improve quality of life and/or longevity without expectation of cure
- Symptom palliation

Systemic therapy has established curative potential for the subset of patients with favourable biologic features (IGVH mutated status and no TP53 dysfunction), and can be considered in younger, fit patients with adequate renal function.

In patients with significant comorbidities or impaired organ function, less intensive chemoimmunotherapy is also available. These treatments can be life-prolonging but do not have curative potential. Note due to poor efficacy, chemotherapy is not recommended for patients with TP53 mutation or del(17p).

Allogeneic bone marrow transplant can cure patients with CLL but is rarely indicated.

Targeted therapies and immunotherapy

are the preferred treatment approach in all patients with TP53 mutation or del(17p) and can be considered in other patient subgroups.

Radiation therapy can be used to treat obstructive/bulky nodes or massive enlargement of the spleen causing symptoms, or to reduce symptoms during palliative treatment.

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.

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

Systemic therapy treatment is rarely urgent. Timing should be discussed to align with the patient's preferences but not delayed to the point where impaired performance status, compromised organ function or recurrent severe infections occur.

Radiation therapy should start **within 72 hours** where organ preservation is the goal. For symptomatic/palliative goals, timing is guided by the severity of the relevant symptoms but is rarely urgent and can start **within 2 weeks** in most cases.

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.

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 refractory, relapsed, residual or progressive disease

Detection

Most relapsed or 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.

Endorsed by:

ALLG <www.allg.org.au> ANZTCT <www.anztct.org.au> Cancer Council <www.cancer.org.au>

HSANZ <www.hsanz.org.au> Leukaemia Foundation <www.leukaemia.org.au>

Lymphoma Australia <www.lymphoma.org.au>