Optimal care pathway for people with AL Amyloidosis

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 AL Amyloidosis*.

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

Step 1: Prevention and early detection

Prevention

The cause of AL amyloidosis is unknown, and there are currently no effective prevention strategies.

Risk factors

- age (occurs mainly in people aged over 40)
- gender (slightly more common in males)
- a pre-existing monoclonal gammopathy (small proportion go onto to develop AL amyloidosis).

Of those with a monoclonal gammopathy, structural changes to immunoglobulin light chains make them more likely to misfold and form amyloid fibrils.

Early detection

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

For patients with a known diagnosis of a monoclonal gammopathy (MGUS, smouldering myeloma, multiple myeloma) a high index of clinical suspicion and careful assessment can facilitate early diagnosis of AL amyloidosis.

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

AL amyloidosis is a multi-organ disease and can present with many otherwise unexplained, non-specific symptoms and/or blood test abnormalities, as well as end-organ complications. As the symptoms are variable and also observed in other more common conditions such as diabetes mellitus, the diagnosis of AL amyloidosis can easily be overlooked which contributes to delayed diagnosis.

Symptoms and signs can include heart failure, fatigue, near-syncope, postural hypotension, oedema, raccoon eyes, macroglossia, carpal tunnel syndrome, peripheral neuropathy, dyspnoea, weight loss, indigestion, renal impairment, proteinuria, hepatomegaly, jaw claudication and gastrointestinal bleeding. The symptoms and signs reflect the presence and extent of organ involvement by amyloidosis.

Common clinical presentations, particularly if they occur concurrently, that raise the suspicion of amyloidosis include:

- heart failure with preserved ejection fraction
- nephrotic syndrome
- peripheral neuropathy, especially rapidly progressive neuropathy and/or autonomic neuropathy
- hepatomegaly with normal imaging appearance.

In most patients more than one organ is affected (most frequently the heart, kidneys, gastrointestinal tract, nervous system and liver), however, some patients may only have one affected organ. Soft tissue involvement such as macroglossia and periorbital purpura are highly suggestive of AL amyloidosis but are uncommon (occurring in only 10%).

Checklist

- ❑ Unexplained, non-specific symptoms, such as fatigue and weight loss, and/or blood abnormalities, as well as end-organ complications.
- ❑ Signs and symptoms recorded
- ❑ Patient notified of support services such as Cancer Council 13 11 20, Leukaemia Foundation 1800 620 420, Australian Amyloidosis Network <www.AAN.org.au> and Myeloma Australia 1800 693 566
- ❑ Referral options discussed with the patient and/or carer including cost implications

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Step 2: Presentation, initial investigations and referral continued

Initial investigations by the GP should include:

The role of the general practitioner is to suspect the patient has a disease that requires a detailed history and examination that may be followed by basic investigations to help identify the organ system/s that require specialist assessment.

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, Australian Amyloidosis Network <www.AAN.org.au> and Myeloma Australia 1800 693 566.

Timeframe

The timing for specialist referral is guided by the severity and type of organ dysfunction. Heart failure, nephrotic syndrome or deteriorating kidney function should be seen by the appropriate specialist **within 1 week**.

For less severe cases to be seen by a specialist physician, the appropriate time frame is **4 weeks**.

Step 3: Diagnosis, staging and treatment planning

If AL amyloidosis is suspected, the following initial investigations are indicated. If these tests are all negative, a diagnosis of AL amyloidosis is extremely unlikely:

- serum and urine protein electrophoresis and immunofixation
- serum free light chains.

A diagnosis of systemic AL amyloidosis requires a tissue biopsy (with Congo Red stain or electron microscopy if available).

- targeted biopsy of an affected organ has the highest sensitivity for diagnosing amyloidosis
- the biopsy can be at a peripheral 'distant' screening tissue (abdominal fat aspirate, rectum, bone marrow, gingiva, salivary gland, etc) but the sensitivity of these biopsies is significantly lower. If there is a high clinical suspicion of amyloidosis and the initial distant site screening biopsies are negative, then the clinically affected organ should be biopsied.

Once AL amyloidosis is suspected or confirmed by tissue biopsy, prompt referral to a haematologist or specialist centre is required for AL subtype confirmation, completion of staging investigations and treatment planning.

Treatment planning

Treatment will depend on several factors, including age, stage, comorbidities, frailty and patient choice. The multidisciplinary team should discuss patients with AL amyloidosis 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 AL Amyloidosis.

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.

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, Australian Amyloidosis Network and Myeloma Australia)
- ❑ Treatment costs discussed with the patient and/or carer

Timeframe

If AL amyloidosis is suspected, diagnostic and staging investigations should be completed **within 4 weeks** of the first consultation by the haematologist or specialist treating centre, or sooner depending on clinical urgency.

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 4: Treatment

Establish intent of treatment

The natural history of AL amyloidosis is complex, and treatment aims may change throughout the disease course. Effective treatments can result in removal of amyloid deposition and recovery of organ function. It's important to note that the monoclonal gammopathy that underlies AL amyloidosis is generally not curable, and many patients will eventually relapse after each line of therapy.

The intent of treatment can include:

- to obtain deep remission with the aim of reversing amyloid deposition and improving the function of organs affected by the amyloidosis
- to improve quality of life and/or longevity
- symptom palliation.

The treatment intent should be established in a multidisciplinary setting, documented in the patient's medical record and conveyed to the patient and carer as appropriate.

Systemic therapy will be suitable for most patients diagnosed with AL amyloidosis with the aim of preventing early death, improving organ function and prolonging survival. Prompt initiation of anti-plasma cell therapy is essential.

Induction therapy can include a combination of proteasome inhibitors, chemotherapy, monoclonal antibodies or corticosteroids and aims to rapidly reduce the amyloidogenic free light chain by directly targeting the underlying plasma cell clone. Patients with IgM-related AL Amyloidosis require therapy directed against the underlying lymphoid clone, most commonly a lymphoplasmacytic clone with treatment adapted from Waldenström macroglobulinemia (WM).

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

Systemic therapy should start **within 4 weeks** of diagnosis particularly if there is cardiac and/or renal disease.

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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 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 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 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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