

# AL amyloidosis

## A Patients' Guide

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MYELOMA PATIENTS EUROPE

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Myeloma Patients Europe AISBL  
Avenue Louise 143/4  
1050 Brussels  
Belgium  
[www.mpeurope.org](http://www.mpeurope.org)  
[info@mpeurope.org](mailto:info@mpeurope.org)



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# 1. Introduction

AL amyloidosis is the most common form of systemic amyloid disease. However, it is still considered a rare condition, with an incidence rate of approximately one case per 80,000-330,000 people in Europe and the USA and most people have never heard of AL amyloidosis. Therefore, you may have a lot of questions. This guide provides answers to the most common ones that you may have upon receiving a diagnosis of AL amyloidosis.

Learning about AL amyloidosis will help you to cope with all the feelings that have come with the diagnosis.



# 2. Amyloidosis

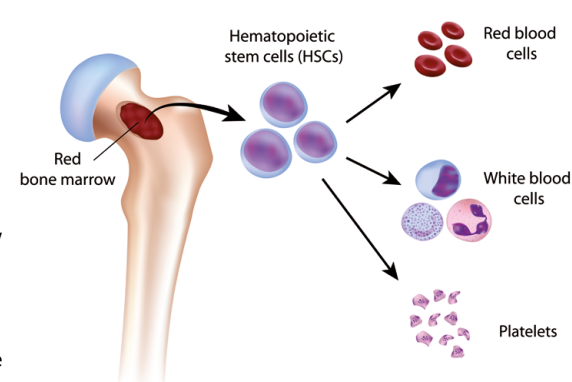
## 2.1 What is amyloidosis?

Amyloidosis is a group of rare diseases with similar characteristics. Amyloidosis occurs when soluble proteins misshape and bind together giving rise to insoluble aggregates, called amyloid fibrils, which deposit in organs and tissues and interfere with their normal functioning. Several different proteins can form amyloid fibrils, and the type of protein determines the disease (for example, localised amyloid precursor proteins deposit in the brain in Alzheimer's disease). The body cannot degrade these thread-like structures and without treatment amyloidosis may lead to life-threatening organ failure. There are several types of amyloidosis; AL (primary amyloidosis), AA (secondary amyloidosis) familial ATTR amyloidosis and wild-type (senile) ATTR amyloidosis.

Some types of amyloidosis are closely related to other conditions ranging from inflammatory diseases (rheumatoid arthritis, chronic infections, Crohn's disease) to haematological malignancies such as multiple myeloma, Waldenström macroglobulinemia and chronic lymphocytic leukemia.

## 2.2 What is bone marrow and what does it do?

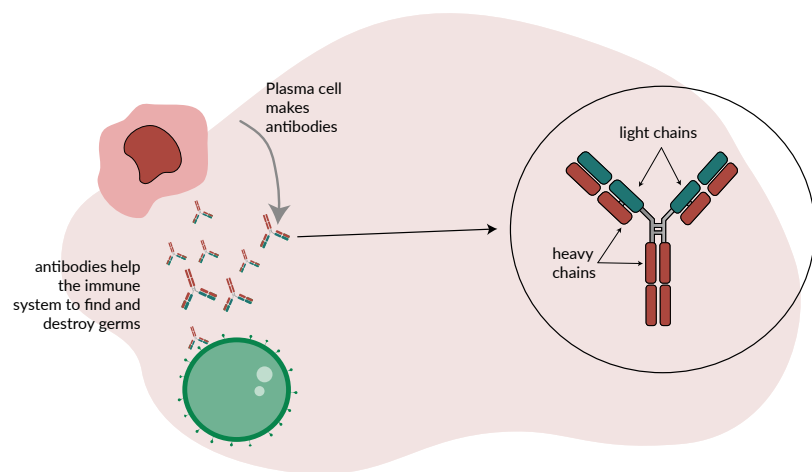
The outside of bones is very hard and dense, but the inner layer of larger bones, like the spine, skull, pelvis, shoulders and the heads of long bones, is made of spongy bone marrow. The bone marrow is the production site for red and white blood cells – the two main types of cells that circulate in the blood. Platelets are also





produced in the bone marrow as fragments of megakaryocytes. One type of white blood cell is known as plasma. Plasma cells produce antibodies (immunoglobulins) to fight infection and are an important component of the body's immune system.

Antibodies are made up of two different kinds of proteins, called heavy chains (which are larger, in red) and light chains (smaller, in green). An antibody has a Y-shaped structure made up of two identical heavy chains and two identical light chains. There are five different types of heavy chains, called G, A, M, D or E; they are usually described as IgG (standing for immunoglobulin G), IgA, IgM, IgD or IgE. The light chains are either  $\kappa$  (kappa) or  $\lambda$  (lambda).



## 2.3 AL amyloidosis

AL amyloidosis (also referred to as light chain amyloidosis) is a rare disease that arises from abnormal plasma cells, which are a type of immune cell responsible for antibodies production. It is a disease of the bone marrow, which affects the organs outside it. In the bone marrow of AL amyloidosis patients, a plasma cell clone composed of abnormal plasma cells produces misfolded immunoglobulin light chains. These aberrant antibodies serve no purpose in the body and deposit in organs and tissues where they interfere with normal functioning. Amyloid proteins disrupt normal functioning because the body is unable to remove them, which leads to the accumulation of these proteins. Specifically, the accumulation of these proteins in vital organs such as the heart, kidneys, liver and gastrointestinal system can cause severe organ dysfunction.

## 2.4 What causes AL amyloidosis

Plasma cells are immune cells that originate from the bone marrow and usually produce normal antibodies (made up of heavy and light chain fragments) to fight infections. In AL amyloidosis, instead of producing normal antibodies, plasma cells produce abnormal and misfolded light chains known as amyloid proteins. These amyloid proteins then aggregate and form fibrils, which deposit in tissues. Furthermore, they are toxic and thus disrupt normal organ function.

The risk factors for AL amyloidosis are poorly understood and this is in part due to the rarity of the condition. However, the risk of developing AL amyloidosis seems to increase with age (most patients diagnosed with the condition are over 60 years old) and the condition is more common in men than in women. Moreover, 10-15% of multiple myeloma patients are subsequently at risk of developing AL amyloidosis.

## 2.5 How common is AL amyloidosis?

AL amyloidosis is a rare disease, with an estimated incidence of nine cases per million person-years. It affects men slightly more often than women and the average age of diagnosed patients is 63 years. In Europe and the USA, the prevalence of AL amyloidosis is between 1/17,000-50,000 people. However, it is assumed that the true figure may be higher due to misdiagnosis because several clinical scenarios can look very similar to this condition.

## 2.6 Stages of AL amyloidosis

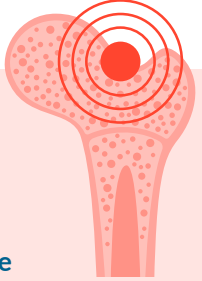
Usually, the doctor will try to determine the stage of the disease to make certain decisions about the treatment and management of your condition. There are different staging methods used across the world. The most commonly used staging of AL amyloidosis monitors heart and kidney function. They usually rely on a number of biomarkers (a biomarker is a biological feature of the body that can be measured by looking at the presence, or absence, and rate of a certain molecule) or clinical measurements. The number of clinical features that are over what is considered normal will determine which stage your illness is in. Stages go from stage I to stage III or IV (depending on the staging system) where higher stages are linked to poorer prognosis.

## 2.7 AL amyloidosis and multiple myeloma

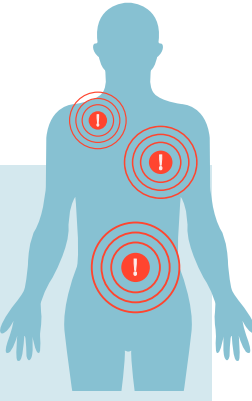
In AL amyloidosis, like in myeloma, abnormal plasma cells in the bone marrow are the source of the pathology. While, on a cellular level, the diseases are similar in AL amyloidosis, unlike myeloma, in the majority of patients, there is no large increase in the number of abnormal plasma cells. AL amyloidosis is not considered to be a cancer. In myeloma, abnormal plasma cells proliferate uncontrollably and produce one type of antibody, known as paraprotein or M-protein, which is made up of heavy and light chains but has no useful function. In AL amyloidosis patients, plasma cells proliferate less, and they produce an abnormal antibody light chain, which is deposited in tissues and organs as amyloid. They also cause/encourage proteotoxic activity against tissue and organs, causing cell damage and even cell death, and affecting cell and organ function. Because these light chains are toxic, lowering their levels is extremely important. As a result of their shared pathophysiology, treatment of both diseases uses the same procedures and drugs, because the goal is to abolish the malignant plasma cell clones.

Furthermore, approximately 10–15% of myeloma patients will develop amyloidosis, and around 30% of patients develop subclinical amyloid deposits, which means the disease is not clinically manifested<sup>5</sup>. In both cases, this disease is called multiple myeloma associated amyloidosis and it is treated in the same way as myeloma.

**AL amyloidosis and myeloma both result from abnormalities of the plasma cells found in the bone marrow**

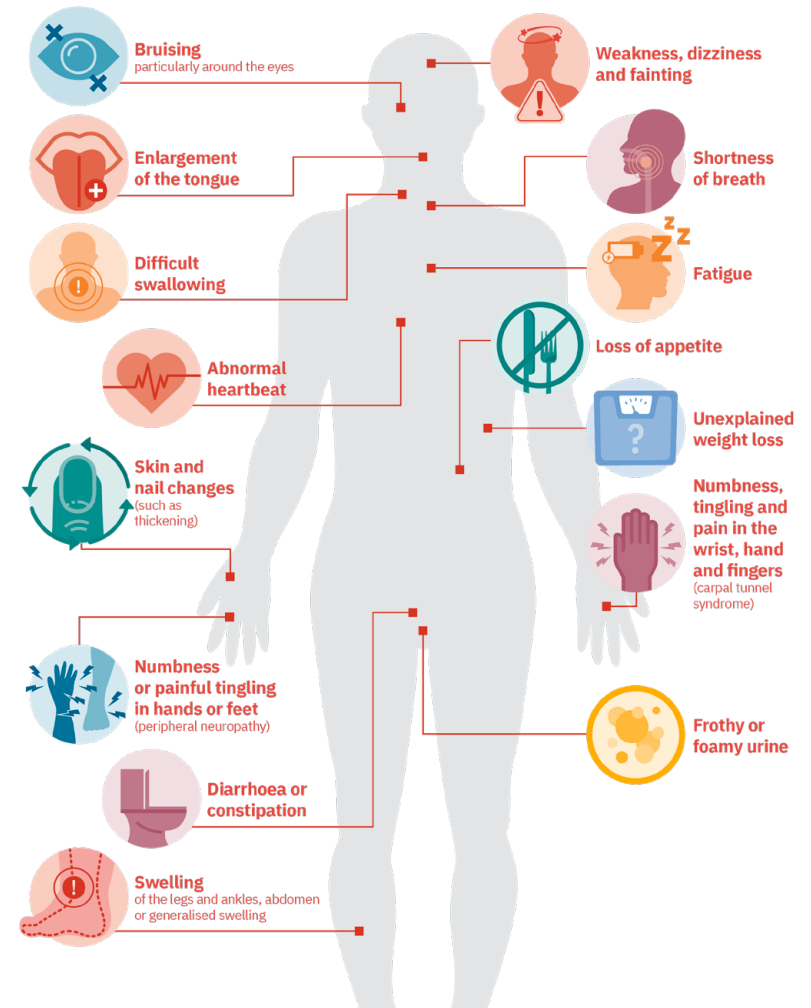


**10-15%** of patients with myeloma may develop symptomatic AL amyloidosis



## 3. Symptoms

Symptoms could be due to AL amyloidosis affecting various organs:



## Heart:

- Shortness of breath: You may experience a tight sensation in the chest and feel the need to breathe more or quicker than usual, especially at exercise such as climbing stairs.
- Palpitations (arrhythmias): Palpitations are feelings or sensations that the heart is racing or pounding. You may experience an unpleasant awareness of your own heartbeat or may feel like your heart skips some beats. You may feel a pounding sensation in the chest, throat, or neck.
- Chest pain: Pain can be experienced as dull, sharp, burning, aching or stabbing feeling.
- Fatigue: You may tire easily, even from day-to-day activities that normally would not tire you out.
- Light-headedness: You may feel dizzy or have the feeling that you might faint, especially when standing up.

## Lungs

- Noisy, wheezing, troublesome or uncomfortable breathing.
- Cough.

## Gastro-intestinal tract (mouth, oesophagus, stomach, small intestine, large intestine and anus)

- Poor appetite: You might experience a loss of appetite and struggle to consume enough food.
- Bloating or excessive gas: Symptoms of this include frequent burping and passing of gas, abdominal pain, pressure, or cramps. A feeling of fullness and a visible increase in the size of the abdomen can also be experienced.
- Constipation or diarrhoea: Stools may become loose or bowel movements may decrease.

## Nervous system

- Carpal tunnel syndrome (or median nerve compression): This is a condition characterised by numbness, tingling, or weakness in the hand. It is caused by

pressure on the median nerve, which is found in the arm and hand, and passes through the wrist inside the carpal tunnel.

- Peripheral neuropathy: This is experienced when damage occurs to the nerves located outside of the brain and spinal cord. It is usually felt as numbness, burning and/or tingling in the hands or feet.
- Autonomic neuropathy: low blood pressure when standing up, difficulty swallowing, difficulty urinating.
- Muscle weakness: Muscle weakness is especially common in the legs.

## Liver

- Enlarged liver (hepatomegaly): This means that the liver is swollen to a larger size than usual.

## Kidney

- Excessive bubbles in the urine: Your urine may become foamy, which can be a sign of protein in the urine; this can indicate kidney abnormalities.
- Decreased urination: You may urinate less than normal.
- Nocturia: You may feel the need to get up at night to urinate.

## Other symptoms

- Brittle nails: Fingernails and toenails may become weaker and break more easily.
- Oedema: Your feet or legs may become visibly swollen.
- Bruising or bleeding easily.
- Purple colour in skin folds.
- Periorbital purpura: The eyelids and/or around the eyes may become purple in colour.
- Macroglossia: Your tongue can become enlarged, if the disease affects the oral tissues.
- Painfull joints.

## 4. Diagnosis

Because the above symptoms are non-specific, it is possible for diagnosis to be delayed by more than a year from the onset of symptoms. Diagnosis of AL amyloidosis may involve several tests, including blood tests, urine tests, imaging and (required in all cases) a biopsy with to identify light chain amyloid deposits. Biopsies and bone marrow tests are necessary to confirm the diagnosis of amyloidosis, and determine what type of amyloidosis a patient has. Blood and urine tests are useful for establishing that amyloid is present, while specialised testing of organs may be required to determine the extent of damage to the organs affected by the disease. Early diagnosis of AL amyloidosis is paramount, because early treatment may prevent or mitigate further organ damage.

### 4.1 Blood and urine tests

There are several kinds of blood and urine tests that can be performed to aid the diagnosis of amyloidosis and determine treatment response once the diagnosis has been established. They are also helpful in identifying which organs are affected by the condition and to investigate the severity of organ damage. Examples of such tests are:

- Assessing protein levels in the urine: samples are collected in a 24-hour period to determine the protein levels in the patient's urine. Excess protein in the urine (proteinuria) can indicate that the kidneys are affected by the disease, which can lead to kidney damage and, ultimately, kidney failure.
- Assessing ALP (alkaline phosphatase) levels in blood: in the blood may be assessed. ALP is an enzyme present throughout the body, which is needed for the breakdown of proteins, an important part of healthy cell and tissue function. Abnormal ALP levels most often indicate a liver involvement.
- Assessing heart function (biomarker): A biomarker is a biological feature of the body that can be measured by looking at the presence (or absence) and rate of a certain molecule. Blood tests can be used to assess the function of the heart. Examples of these biomarker tests are: troponin T, troponin I, NT-proBNP (which stands for N-terminal pro-brain natriuretic peptide)

and BNP (brain natriuretic peptide). These markers are diagnostic tools for cardiac involvement with high sensitivity and can detect early disease (without symptoms).

- Testing abnormal antibody (immunoglobulin) in blood: Such as the serum free light chain (FLC) test. This test allows the assessment of kappa and lambda light chain levels that make up the abnormal amyloid fibrils.
- Immunofixation and electrophoresis: This test can be done on blood or urine samples. It allows the measurement of abnormal monoclonal proteins, M proteins.

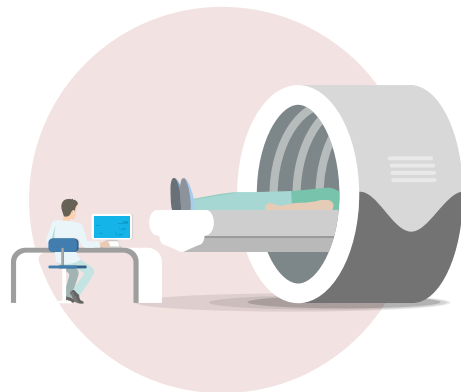
The collection of urine samples is a straightforward process, although somewhat cumbersome in the case of 24-hour urine samples. For a test using blood, the nurse will insert a needle into a vein in the arm and extract several vials of blood. The amount withdrawn depends on the laboratory technology and protocol applied: it is usually between 30ml and 50ml distributed across several vials.

### 4.2 Echocardiogram and imaging

An echocardiogram (or “echo”) is a type of ultrasound scan used to look at the heart and nearby blood vessels. Echocardiograms use a device that emits ultrasound and measures its reflection from the organs in the body. The doctor or technician applies a gliding lubricant to the area where the scan is performed, and then carefully moves the ultrasound device around the skin. Amyloid deposits in the heart cannot be visualised with an echocardiogram but it can detect thickened cardiac walls that also do not relax as should be.

Alternatively, magnetic resonance imaging (MRI) can be useful for visualising certain aspects that are very specific to amyloid deposits. The reflections from the internal organs are processed by a computer to generate an image. The patient may be administered a contrast agent and is then placed in an MRI machine. The machine emits magnetic rays at high speed that are reflected from the cells in the body. An elaborated computer model is used to measure these reflected waves and to construct a three-dimensional image of the internal organs and their possible visible changes. Some patients may find the MRI examination uncomfortable as they have to spend a relatively long time not moving and confined to a narrow tube inside the MRI device. It is also a noisy examination as the device uses large magnets rotating at high speeds. Both of these imaging techniques are relatively easy and cause no pain.

Another important imaging technique is referred to as an SAP scan. SAP stands for serum amyloid P component. During this test, the patient receives an injection of this component together with a labelling agent. The amyloid deposits can then be visualised with a scanning method, thus determining the size and location of the deposits. This test is only available in few countries such as the Netherlands and the UK, so it is not mandatory for a complete clinical assessment.



### 4.3 Tissue biopsies

A biopsy is taking small sample of tissue. This is often taken under the skin of the periumbilical (around your belly button) area (abdominal fat biopsy or fat pad aspiration). Abdominal fat biopsies are relatively easy and not particularly painful. Alternatively, a biopsy can also be taken from the organ affected by amyloid deposits. However, biopsies from other internal organs can be complicated and painful as well, and so this diagnostic method should be used sparingly. Another possible valid approach is to obtain a small salivary gland biopsy.

During biopsy, a long needle is inserted into the organ to be examined and a small amount of tissue is extracted for the test. This may be painful or uncomfortable. The tissue samples are then stained with a dye called “Congo red stain” and examined under a microscope. Congo red reacts with the amyloid proteins for visualisation. Once amyloid fibrils are detected, to distinguish between the different form of amyloidosis, a typing of amyloid protein must be performed. There are two main tests used to characterise amyloid deposits: immunoelectron microscopy and mass spectrometry.

### 4.4 Bone marrow tests

Bone marrow samples are used to find the abnormal cells producing the free light chains. There are two types of bone marrow samples: a bone marrow aspirate (BMA) involves fluid aspiration from the bone marrow, while a bone

marrow biopsy (BMB) removes a small piece of bone marrow tissue. However, bone marrow aspirates are not advised in AL amyloidosis because an aspirate cannot be examined for amyloid presence. During this procedure, which can be done on an outpatient basis, a long needle is inserted into one of your larger bones, usually the pelvis, and a small amount of bone marrow is obtained. Bone marrow biopsies can be particularly challenging and painful. Local anaesthesia will be performed during the procedure to numb the area of needle insertion. In some cases, you may receive sedation for the time of the test to reduce your pain. You may also experience pain at the biopsy site for several days after the procedure. In the laboratory, Congo red staining can only be performed on bone marrow biopsy samples to determine if amyloid is present.

### 4.5 Specialised testing of affected organs

If signs of organ involvement are detected throughout initial testing (for example, by looking at blood and urine samples), doctors may decide to carry out biopsies taken from these organs or perform other diagnostic methods (such as an echocardiogram to investigate heart health) to determine the extent and severity of organ damage.

### 4.6 Prognosis

Prognosis refers to the forecast or anticipated course of a medical condition. The prognosis of AL amyloidosis is highly dependent on a patient’s response to treatment and the extent of organ damage at diagnosis. Specifically, the extent and severity of heart involvement is considered a significant determinant of the prognosis of AL amyloidosis. When significant damage to the heart is already present at the point of diagnosis, patients generally have a poor prognostic outlook (with a high risk of death within a few months). Additionally, life expectancy varies according to the stage of the disease. Early diagnosis is therefore extremely important in order to achieve the best possible treatment outcome and prognosis. Prolonged survival is possible when treatment commences early in the course of disease and the patient responds well to treatment. For all these reasons the current median survival varies a lot between individual patients, from three months to several years, and this may evolve rapidly with the discovery of new treatments.

## 5. Treatment

Since AL amyloidosis is a disease which manifests quite differently from patient to patient, treatment is highly individualised as well. The chosen treatment approach will largely be determined by the progression and severity of the disease, and by the affected organs. The two most important goals of treatment are 1) symptom management and 2) minimising or stopping the production of amyloid proteins. By reducing light chains to normal levels, the direct toxicity is ameliorated, and organ-related symptoms such as heart failure may improve even if the Echo test shows no change.

### 5.1 Treatment options

Treatment approach depends on the type of amyloid deposit and on the underlining disease (if present). Although amyloidosis is not a cancer, treatments may include the use of chemotherapy drugs that are mostly used to treat cancers. Organ or stem cell transplants are in some cases beneficial as well. As both myeloma and AL amyloidosis are caused by the presence of an abnormal plasma cell clone, drugs effective against myeloma may also benefit AL amyloidosis patients. To date, the only approved therapy specifically for the treatment of AL amyloidosis is the combination of the immunotherapy drug daratumumab and chemotherapy drugs cyclophosphamide and bortezomib with the corticosteroid dexamethasone (Dara-CyBorD). Further effective combinations that your doctor may recommend are bortezomib, the chemotherapy drug melphalan and dexamethasone (BMDex), as well as cyclophosphamide, bortezomib and dexamethasone (CyBorD).

An autologous stem cell transplant (ASCT) involves the use of your own blood stem cells to replace your bone marrow. This approach is often effective because it leads to the eradication of the plasma cells producing amyloid protein. ASCT can significantly prolong survival, though, only approximately 20% of patients qualify for this, as you need to be quite fit to safely undergo the procedure.

Reversal of organ damage, as well as the removal of amyloid deposits that are already present in tissues is challenging. However, there are some promising novel drugs in clinical trials that are designed to enable the removal of amyloid deposits (see *Clinical trials* section).

### 5.2 How is treatment response measured?

Treatment response is measured regularly, using the same types of tests that are applied to diagnose AL amyloidosis, including blood tests, urine tests, imaging and biopsies (see *Diagnosis* section). It is important to recall that hematologic and organ response criteria are now based on biomarkers and validated criteria are defined.





## 6. Living with AL amyloidosis

### 6.1 Coping with symptoms

The symptoms of AL amyloidosis vary from patient to patient and largely depend on which organs are affected by the condition. Generally speaking, however, it is important that you take care of your general health and consult your doctor and healthcare team about any observed changes to your well-being. If they are aware of any symptoms or treatment side effects you are experiencing, they may be able to help you manage them, or prescribe medications to alleviate them. Symptoms and treatment side effects can largely overlap; a more detailed description of these can be found in the *Coping with symptoms and treatment side effects* section.

### 6.2 Coping with the diagnosis

Your reaction to receiving a diagnosis of AL amyloidosis may vary from feeling a sense of shock, anxiety, feeling overcome or numb, or you may feel angry or frustrated. All of these emotional reactions are completely natural. It is also normal to feel a sense of slight relief, because at last you have found an explanation for how you've been feeling and find it better to know than to worry. This is a very natural reaction too.

The diagnosis may provide a chance to appraise what is most important to you as well, and could bring you closer to your partner, family and friends. It may also prompt questions about how long you can expect to live. This is very hard to answer, as that is largely determined by which of your organs are affected and to what extent, as well as by how well you respond to treatment.

It can be very helpful to learn about the disease, so that you understand more clearly what your diagnosis means, and so that you are able to formulate what you need to ask your doctors. It will also help you to talk to your family, as they will also try to understand more about AL amyloidosis. Take your own time to find out about AL amyloidosis, as it is easy to become overwhelmed. If you look for information sources on the internet, it's important to find reliable sources such as medical organisations, rather than websites where you read opinions

that may not be reliable. Also remember that the information you find online should supplement - and not replace - the advice and guidance from your medical team, which is designed for you as an individual.

It can, of course, feel very difficult to explain to the people close to you that you have AL amyloidosis. It may help if you tell one or two and ask them to explain it to the other people you feel will need to know. Some patients find it easier to tell people by phone rather than face-to-face.

Talking about the disease with those closest to you can be a great source of support and help, and may prevent you from feeling isolated. Your partner, family and friends may also be feeling anxious about you and perhaps afraid of upsetting you by asking too much. It does help to talk, not just about the disease but about everyday things as well.

### 6.3 Preparing for medical check-ups

You will have regular check-ups from the time of your diagnosis – the frequency may vary in different countries of Europe, but they are likely to be every few weeks and will be set by your physician.

Because AL amyloidosis is a complicated condition and you may have questions about many aspects of your symptoms, feelings and treatments, it is a good idea to think carefully about what you want to ask before your check-ups, so you can ensure everything is covered. Taking a written list of questions and concerns along for your check-up might be helpful to make sure none of your questions remain unanswered. Taking notes during your appointments is a good idea as well, so you can ensure you have all the necessary information at hand after the check-up.

### 6.4 Caring for yourself

#### *Talking to your doctor*

It is vital to develop good communication with your doctor and healthcare team to maximise the support and efficacy of the treatment you receive. We recommend that you prepare some questions to ask your doctor at your check-up. Many people find that it is helpful to take their partner or friend with them; this can help you to take in and remember the doctor's suggestions. Furthermore, it may be useful to track symptoms, side effects and any changes



to your well-being. Discussing these with your doctor can be very helpful. If your doctor proposes a change in your treatment, it is perfectly acceptable to ask for a little more time to make your decision when you have been able to discuss it with your family.

### **Diet and nutrition**

Your doctor or healthcare team may give you recommendations on what to eat and drink, and what to avoid. It is important to follow a healthy diet if you are an AL amyloidosis patient. Especially how much you may drink a day and the salt and protein content is important. It is advised to consult a dietician.

### **Physical activity and exercise**

Exercise and physical activity may reduce fatigue, feelings of anxiety and depression, and build muscle strength. Although every patient is different, some form of exercise may benefit you. Aerobic exercises (walking, cycling, using a cross trainer etc) must be performed carefully especially in patients with heart involvement. If you are not used to regular physical activity, make sure to speak to your doctor in advance and then build up your routine gradually, while listening to your body and staying within your limits to avoid over-exhausting yourself. A visit to a physiotherapist, who can help to assemble an exercise routine that fits your needs and ability, may be beneficial. The key point to remember when exercising is not to overdo it and only do as much as you feel capable of doing. Stop exercising and consult your doctor, if you experience dizziness or nausea, shortness of breath, sharp or stabbing pain in the chest or any other area of your body.

If certain organs are affected by the disease, this may influence your ability to partake in certain forms of physical activity. Cardiac amyloidosis patients, for example, should take additional care during exercise; you should make sure that you stay below 80% of your maximum heart rate (which is defined by your height, weight and age). If your immune system is weakened due to treatment side effects, you should take care to avoid places where you could easily contract an infection (e.g., saunas). AL amyloidosis can cause your bones and visceral organs (i.e., liver and spleen) to become more brittle, hence, certain sports should be avoided (e.g., contact sports) to minimise the chance of injuring yourself.

### **Sexuality**

Loss of interest in sex is not at all uncommon and may be caused by psychological or emotional factors, such as feeling anxious or exhausted. Alternatively, the

cause may be physical, for example neuropathy caused by AL amyloidosis may lead to erectile dysfunction. Some treatment regimens are also known to possess that side effect. Not wanting to engage in sex can itself cause more stress between partners, if you feel depressed or unattractive, or if you or your partner feel unwanted or rejected.

It's important to talk to your partner, so that you understand each other's feelings, and to make sure that neither of you misinterprets the situation. Once you start to talk, you should be able to find out what level of physical contact feels right for the time being, and then gradually develop that into a fuller intimacy when you are ready. Your doctors and nurses can also offer guidance and support, and they will not be embarrassed if you ask for help. For example, if you suffer from erectile dysfunction due to physical reasons, if your doctor feels it is safe to do, so he/she can prescribe medications (such as sildenafil), which may be helpful.

### **Oral care**

AL amyloidosis may significantly impact oral health. Presence of amyloid protein in the oral tissues may lead to enlargement of the tongue, as well as frequent oral bleeding. Good dental hygiene, using a soft toothbrush, and keeping yourself well hydrated are the best ways to prevent infection in your mouth. Any pain or discomfort in your mouth should be reported to your doctor or nurse and can be relieved with antibiotic or pain-killing mouthwashes, or by specific antifungal or antiviral treatments. You should avoid salty, spicy or acidic foods that can increase soreness.

Certain treatments can increase the risk of mouth ulcers or an inflamed mouth lining. Some other treatments can temporarily lower your blood platelet count, and this can make you more liable to bleed from your gums. You may find that your mouth stays rather dry – this is because treatment may interfere with saliva production, but it can be relieved with an artificial saliva spray.



## 6.5 Coping with symptoms and treatment side effects

### **Appetite loss**

Sometimes you may have a sore mouth from chemotherapy, or simply don't feel like eating, so a meal replacement drink may be easier to consume.

It can also be easier to eat smaller meals, more often than usual, and take a larger meal when you feel able to. Avoid fatty or fried foods and those that are very sweet or spicy. It is important to keep drinking water or other drinks too – milk, squash, decaffeinated tea or coffee each day, or ordinary tea or coffee in moderation.

If these approaches don't help, you can ask to be referred to a dietician, who can recommend some more alternatives.

### **Constipation**

AL amyloidosis itself may result in constipation. Constipation may also arise as a side effect of treatment, so it is important to ask for advice from your doctor or healthcare team to find out the cause. Don't be afraid or embarrassed to tell your doctor about constipation, as they are quite used to this sort of problem and will be able to help resolve what can be a distressing problem with a big impact on your quality of life.

As it is much easier to prevent constipation than to treat it, it is a good idea to make sure that your diet includes some foods that are high in fibre, e.g. bran, wholegrain bread, fruit, vegetables and especially beans or lentils. Cake and white bread should be kept to a minimum; the same goes for sugar-rich foods in general, as simple carbohydrates can cause or worsen constipation. It is also important to make sure that you don't become dehydrated. Use of natural remedies should be discussed with your doctor, too, in case of any interaction with your medication. Finally, gentle exercise like walking, swimming or cycling could be a regular part of your routine but must be performed carefully especially in patients with heart involvement.

If constipation becomes a big problem, your doctor can prescribe several types of laxatives, which either reduce the removal of water from the faeces in the intestine, making them softer, or increase their bulk, or stimulate the movement of the bowel.

### **Diarrhoea**

Diarrhoea is considered as episodes of passing loose or watery bowel motions more than three times a day. It can be accompanied by headache, stomach cramps and loss of appetite or even nausea and vomiting. AL amyloidosis can give rise to diarrhoea due to its disruptive effect on the normal functioning of the gastro-intestinal tract. Some chemotherapy drugs, for example, bortezomib, can also cause diarrhoea, or it can result from an unrelated infection.

If you are experiencing diarrhoea, you should report it to your doctor or healthcare team so the most appropriate treatment can be prescribed. There are also several things you can do yourself that will help. Make sure you drink plenty of water, or diluted fruit juice, and avoid tea and coffee. Keep to small, light meals including chicken, eggs and white fish, and avoid spicy foods.

### **Dysphagia**

Dysphagia refers to difficulty in swallowing solids, liquids or both, and may be associated with coughing or choking while eating or drinking. Dysphagia is a possible side effect after a stem cell transplant. Treatment depends on the symptoms experienced but avoiding meat (which can be hard to swallow) may help, and therapy can help reduce the chance of choking.

### **Fluid retention**

Amyloid proteins can cause damage to the kidneys among other organs. Misfolded light chain proteins can block the kidney tubules, causing them to fail to remove enough waste substances from the blood through urination.

Chronic kidney failure develops over a longer period (weeks or months) and is shown by the presence of protein in the urine (proteinuria); this is caused by the deposition of amyloid protein in the kidneys. The urine shows a high level of albumin, and the blood has a very low level. Fluid retention follows, causing swelling in the legs, ankles or feet. Rapid increase of body weight can be a sign of fluid overload. Other symptoms include tiredness and difficulty breathing.

To reduce the risk of fluid overload, your doctor can recommend that you limit your fluid intake (likely to be around or less than 1.5 litres) and keep your salt intake to a minimum. Daily weight checks can help detect fluid overload and your doctor might ask you to weigh yourself every day - if he/she thinks you are at risk - in order to take appropriate measures. If, despite an appropriate diet and fluid intake limitations, you experience fluid overload, it can be treated with diuretics.

Renal failure is usually treated by dialysis. Preventing the occurrence of kidney failure rather than treating it once it arises is much more viable, so avoid getting dehydrated (to keep the kidneys actively functioning), and using non-steroidal anti-inflammatory drugs (e.g. ibuprofen).

### **Fatigue**

Fatigue is both a common symptom of AL amyloidosis, as well as a regularly experienced side effect of treatment. It can be aggravated by anaemia. Exhaustion can make it difficult to meet even the basic challenges of day-to-day life, however, some approaches may be helpful to mitigate this.

Getting enough sleep is vital. Try to make a routine of going to bed and getting up at the same time, and take a rest during the day when you need to. Gentle exercise can help by improving your appetite and your energy level.

When you need to do certain tasks, spread them out over time instead of trying to do everything at once; focus on whatever is most important or urgent. Accept offers of help from your family and friends – as well as helping you, this will make them feel that they are being useful in some way. If you are working, investigate whether you could work from home, or reduce your hours or responsibilities.

### **Hair loss**

Most chemotherapy drugs used in the treatment of AL amyloidosis cause hair thinning rather than complete loss, which is mainly related to the intensive chemotherapy given before a stem cell transplant. Hair loss happens because the chemotherapy drugs attack all the cells in the body, which are rapidly dividing, and among these are the hair follicles. Hair loss can be distressing, but the hair will grow back within a few months after the treatment is completed. Your new hair may be finer than before, or curlier, or a slightly different colour.

Having your hair cut short before you start to lose it through chemotherapy can work well, as you can feel more of a sense of control while it is thinning and growing back. Otherwise, today's wigs are very natural-looking, or you could use a scarf – and many people choose not to cover their heads at all. It's entirely a matter of what feels right for you.

### **Infertility**

Some of the medications used in the treatment of AL amyloidosis can affect fertility. Hence, it is vital to consult your doctor in case you are planning to have

children in the future. The infertility caused by treatment is often temporary but could be permanent depending on which drugs you are given. Those most likely to affect fertility are cyclophosphamide and melphalan, and permanent infertility is more likely with higher doses, like those given just before a stem cell transplant.

Your doctor may be able to refer you to a fertility specialist to discuss what can be done. It may be possible to undergo sperm or egg collection for later use, and fertility counsellors can provide supportive advice. Reimbursement for these procedures varies from one country to another; you can ask your doctors what your healthcare system's options are.

### **Nausea and vomiting**

Side effects from chemotherapy drugs (e.g., bortezomib) may include nausea and vomiting. Infections that arise when treatment suppresses the immune system can also cause nausea and vomiting. In case these are chemotherapy-related, they can be treated with anti-emetics. If they are caused by an infection, antibiotics may be needed. Aside from drug treatment, it can be helpful to eat small, frequent meals and avoid foods that are fatty, spicy or have a strong smell, as these may further aggravate your nausea or upset your stomach.



### **Neutropaenia**

Chemotherapy may result in a lower level of neutrophils (a type of white blood cell) in the blood, and a shortage of neutrophils is referred to as neutropaenia. This may put you at greater risk than normal of food poisoning caused by bacterial or fungal contamination. There is also an increased risk of other kinds of bacterial infections such as pneumonia or urinary tract infection. The risk is

also increased because the lining of the gut can be damaged by chemotherapy, which makes it easier for bacteria in food to enter the bloodstream.

If you develop neutropaenia, you will be given detailed advice by your doctor or dietician about which foods to avoid and which are good alternatives. In addition, avoiding crowded areas is also important when trying to prevent infection. The strictness of this advice depends on your level of neutrophils. You may need to continue following this guidance even after your neutrophil count has recovered, as you may still be at a higher risk of infection.

The main foods to avoid are unpasteurised dairy products (like farm-fresh milk); soft or blue cheeses; raw or lightly cooked shellfish; raw, undercooked or smoked meat, poultry or fish; raw or undercooked eggs (or foods that contain them, like sauces or ice-cream); foods, drinks and supplements described as 'probiotic' or 'bio', and meat or vegetable pates.

You will also need to follow a high level of food safety hygiene practices in everything related to your food – shopping, food preparation and storage. There are many points to take into account, and you will be given detailed guidance. For example, avoid buying food with damaged packaging and avoid large packets that will be open for longer, and could increase the chance of contamination. Always store raw and cooked foods separately and make sure that frozen food is defrosted, covered and at the bottom of the fridge (rather than at room temperature), to avoid it dripping onto other food. Cook all food thoroughly until it is piping hot all the way through and the meat juices run clear. Take care with hand hygiene too: always wash your hands before preparing food and after touching your hair, pets, rubbish, dirty laundry and visiting the toilet. Keep a separate chopping board for raw meat or fish and do not use it for other foods.

Granulocyte-colony stimulating factor (G-CSF) is a medication that may be administered to hasten neutrophil recovery. G-CSF is mostly given via an injection under the skin. It can also be injected into the bloodstream (intravenously).

### **Pain**

Any form of pain or discomfort, regardless of whether it arises as a symptom of the disease itself or as a side effect of therapy, should be reported to your doctor or healthcare team, as they may be able to prescribe medication to lessen or alleviate your discomfort, or evaluate what the cause is.

### **Peripheral neuropathy**

Damage to the peripheral nervous system (PNS) is referred to as peripheral neuropathy. The PNS includes all the nerves in the body except the brain and spinal cord. These nerves communicate between the brain and the other parts of the body, and are composed of two types of specialised cells: motor neurons and sensory neurons. The motor neurons carry electrical impulses from the brain to the muscles and enable them to carry out movement by contracting or relaxing. The sensory neurons carry information about the sensations of pain and touch to the brain from all external parts of the body. When these sensory neurons are damaged in peripheral neuropathy, the sensory messages can be distorted or interrupted, which the brain interprets as tingling, numbness, altered sensation, increased sensitivity to touch, or pain. The sensations are most often felt in the hands and feet.

Peripheral neuropathy may occur as a result of the deposition of amyloid protein in and around the nerves, or as a side effect of treatment, for example, bortezomib can cause peripheral nerve damage.

The treatment for peripheral neuropathy depends on its cause. If it is caused by the disease, then treatment may reduce the neuropathy. If it has arisen as a side effect, then the treatment concerned can be stopped or given at a reduced dose. If it is a side effect of bortezomib, it may be sufficient to change from intravenous to subcutaneous administration (injection into the skin rather than into a vein).

Pain from peripheral neuropathy can be relieved by a range of drugs, including amitriptyline, gabapentin or carbamazepine, by local anaesthetic, or by a TENS machine (transcutaneous electrical nerve stimulation), which delivers tiny electrical impulses to the nerves in the skin.

### **Skin conditions**

Some chemotherapy drugs (e.g., bortezomib) can result in a rash and dry, itchy skin rashes. If this happens, the medication should be reduced or withdrawn.

### **Thrombocytopenia**

Blood platelets are vital for the blood clotting process. Consequently, a low level of platelets in the blood can make you more prone to bleeding or bruising. Having a below normal level of platelets is known as thrombocytopenia. This may arise as a side effect of treatment with bortezomib, cyclophosphamide and melphalan. Thrombocytopenia may give no symptoms at all, or spontaneous bleeding from

the gums or nose, extended bleeding from cuts, excessive bruising, or a red rash of tiny pinpoint marks, commonly in the lower legs. If the thrombocytopaenia develops as a side effect of treatment, it may be necessary to reduce the dose, or delay treatment until your platelet level recovers.

You should watch for any unusual bleeding and report it to your doctor. It is also a good idea to avoid anything that could give rise to bleeding or bruising, and to use a soft toothbrush to avoid damaging your gums. Limiting alcohol intake is helpful too, as alcohol tends to reduce the platelet level and 'thin' the blood. If you see blood in your urine, stools or vomit, report it immediately to your doctor.

## 6.6 Coping with the socio-economical impact

### *Managing work and AL amyloidosis*

If you are diagnosed with AL amyloidosis, you might want to discuss this with your employer. A doctor or nurse can provide written confirmation of the diagnosis and may also be able to provide an explanation on how this may affect your ability to work. It may be necessary to take time off for tests and treatments, possibly involving inpatient hospital stays. Many employers may be open to taking on a more flexible approach towards working hours and conditions, and reducing the level of responsibility at work in case that might be required.

Caring for dependents, like children or elderly parents, may become difficult for patients and it might be worthwhile to make some other plans for their care, for example, arranging for someone to care for them in case you need to go to hospital for some time. These plans may not need to be implemented, but their existence can be reassuring, and in case you may need to go to hospital at short notice for treatment or care, such plans may prove to be very useful.

### *Insurance, financial and other issues*

Living with AL amyloidosis, as well as treatment approaches may make it difficult for you to stay in the working environment. It may become necessary to take a significant amount of time off work or quit, which can give rise to financial worries and difficulties. However, governmental support may be available, and patients are often eligible for a number of benefits. These vary from country to country, but in many cases provide for a living or personal independence allowance, support to pay for a carer, or a tax allowance. If you continue working, you may be entitled to a statutory support allowance, if you are not eligible for sick pay from your employer. Relatives or friends looking after you may be able to claim a carer's allowance.

Advice on the various available benefits can usually be obtained from nurses and social workers at your hospital, or from community, patient or citizen groups, or online.

### *Getting help and looking for resources*

You can find support and information from many sources. First and foremost, your own medical team should be your main reference source, as only the members of this team will have full knowledge of your individual condition and what treatments are working, or have been less successful.

This team will include your consultant haematologist, specialist nurses and general practitioner. Depending on your exact combination of symptoms, you may also be advised by specialists in particular systems of the body, e.g., a renal specialist, if you have kidney problems, or a neurologist, if you have neuropathy. You should also have access to social workers or a community advice bureau for questions relating to social care or finance.



You may find that information from the internet is variable in its quality and level of detail, and healthcare systems also vary slightly different in every country. An excellent starting point for information relevant to your own country is the website of your own national amyloidosis association (if one exists in your country), or Myeloma Patients Europe. Many of these associations can put you in touch with support groups where you can talk and exchange experiences and problems with other patients, and also professionals. Some have online discussion forums, where you can chat with patients wherever they live. Patient



organisations can provide access to valuable information about the disease and treatment options, which healthcare professionals to turn to, self-caring and career suggestions etc. They might be hosting social events as well, and attending these can be a motivating, informative and positive experience. Examples of such groups are:

- **Austria.** Leben mit Amyloidose: [www.amyloidosis-austria.at](http://www.amyloidosis-austria.at)
- **France.** Association Française contre l’Amylose : [www.amylose.asso.fr](http://www.amylose.asso.fr)
- **Germany.** Amyloidose Selbsthilfegruppe: [www.amyloidose-selbsthilfe.de](http://www.amyloidose-selbsthilfe.de)
- **Israel.** Amyloidosis Israel: [www.amyloidosis.org.il](http://www.amyloidosis.org.il)
- **Italy.** Associazione Italiana contro leucemi linfomi e mieloma (AIL): [www.ail.it](http://www.ail.it)
- **North Macedonia.** Association for help and support of patients and their caregivers with hematological diseases (HEMA): [www.hema.org.mk](http://www.hema.org.mk)
- **Netherlands.** Amyloidosis Foundation Netherlands (SAN): [www.amyloidose.nl](http://www.amyloidose.nl)
- **Norway.** Blodkreftforeningenn: [www.blodkreftforeningen.no](http://www.blodkreftforeningen.no)
- **Slovakia.** Slovak Myeloma Society (SMYS): [www.myelom.sk](http://www.myelom.sk)
- **Slovenia.** Association of Patients with Blood Diseases Slovenia: [www.drustvo-bkb.si](http://www.drustvo-bkb.si)
- **Spain.** Asociación Española de Amiloidosis (AMILO): [www.amilo.es](http://www.amilo.es)
- **United Kingdom.** Myeloma UK: [www.myeloma.org.uk](http://www.myeloma.org.uk)

Alternatively, you may consider reaching out to an umbrella organisation (like MPE) or other non-profit organisations that represent AL amyloidosis patients for support and information. Examples of such organisations are:

- **Amyloidosis Alliance:** [www.amyloidosisalliance.org](http://www.amyloidosisalliance.org)
- **Amyloidosis Foundation:** [www.amyloidosis.org](http://www.amyloidosis.org)
- **Amyloidosis Research Consortium:** [www.arci.org](http://www.arci.org)

## 7. Palliative care

Palliative care or “palliation” is specialised medical care for people living with a serious illness. It is often confused with the care people receive when they are dying (end-of-life care).

Whilst palliative care can help people at the end of life, it is not just for use in this setting. You may be offered it earlier on in your disease, while you are receiving treatment.

Palliative care focuses on providing relief from the side-effects of treatment, the symptoms and stress of the disease, and supporting you and your family. The main goal is to improve quality of life for both the patient and the family.

The World Health Organisation (WHO) defines this term as “an approach [to treatment] that improves the quality of life of patients and their families who are facing the problems associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and correct assessment and treatment of pain and other problems, whether physical, psychosocial or spiritual.”

You should speak to your healthcare team about accessing support from a palliative care specialist, or other supportive options, as part of your care. This should be done as soon as possible in your treatment pathway, to ensure you access support as soon as possible. This is particularly important if your symptoms are worsening, or you have other issues or concerns. Palliative care is offered in various settings (in a hospital, at home or in a hospice) and may look different depending on what country you live in. If your symptoms are worsening, or you have other issues or concerns and need more support, we suggest you speak with your treating doctor about your options for palliative care, or other supportive care options.

End of life care should help you to live as well as possible. Palliative care is an important part of end of life care and can help reduce your symptoms and improve quality of life. Your healthcare team should ask you about your needs and preferences, and take these into account as they work with you to plan your care. They should also support your family, carers or other people who are

important to you. While difficult, it is never too early to discuss these matters with your loved ones.

## 7.1 Advance decisions: living wills

If you have any wish regarding the treatments that you are willing to accept or refuse at the end of your life, you might want to think about leaving some instructions. A living will or advance decision is a document detailing the wishes of someone. This can be used when someone becomes unable to communicate for themselves. Because it is a legal document, there are some differences in the requirements of individual countries. The following paragraphs explain the purpose of the advance decision; but you will need to check exactly what the provisions are in your own country as individual countries have different policies regarding end of life.

The document must explain exactly which treatments you want to refuse, and in what circumstances (if you might not want to refuse them in all situations). It can be helpful to discuss with a doctor what treatments you might need in future, and what would happen if you refuse them. If you might die as a result of refusing such treatment, the document must state clearly that the advance decision is applicable even if life is at risk or shortened as a result. An advance decision cannot be used to ask for specific treatments, or to ask for help to end your life.

To make your wishes legally valid, they must be written down and signed and dated by yourself, and by a witness. To be put into action, your wishes must be applicable to your situation and the treatments available, if you are not able to make your own decisions about your treatment, e.g., if you are unconscious, and if there is no reason to suspect that you might have changed your mind since the document was signed.

Writing a living will is not something you have to do, or which should cause you any unnecessary stress. You might simply want to discuss these matters with your loved ones to make sure they understand your choices, whenever you feel ready to do so.

## 8. Clinical trials

Clinical trials are studies that are crucial for the development of novel treatment options for AL amyloidosis. For example, therapeutics that can help the body remove amyloid deposits are in clinical trials and show great promise<sup>17</sup>. Clinical trials currently underway in Europe are all listed on the [European Clinical Trials Register](#).

### 8.1 What are clinical trials?

Clinical trials are a series of research studies performed on people. Their aim is to evaluate and compare new medications, combinations of medications, procedures and medical devices and generate information on how safe and effective they would be in practice. They generally progress from small pilot studies to large-scale trials.

Satisfactory results of clinical trials are required by both national and European regulatory agencies before the products or procedures can be granted market authorisation and all the conditions of use agreed. The trials are carried out according to strict procedures (protocols) that have been approved by an independent research ethics committee to protect the interests of the people taking part.

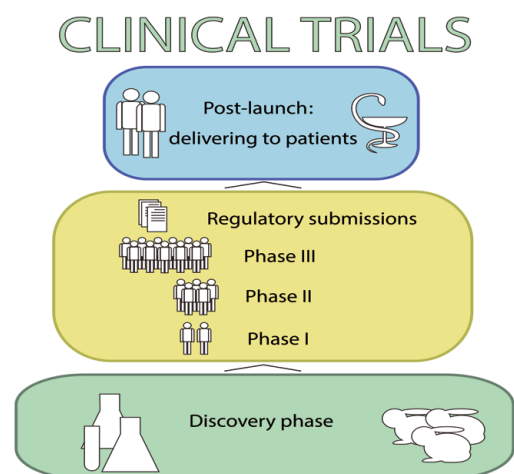
Before a new medication can enter the market and be available to patients, its safety and efficacy must be tested throughout the phases outlined below. Volunteer patients can take part in the trials of new medications, provided they meet the specific conditions of the individual trial, which may include the current state of their disease, recent treatments and their outcome, age, and other health conditions etc. Many people are keen to participate in trials, because as well as giving access to new treatments before they are widely available, taking part will guarantee a high level of monitoring from the clinical staff running the trial.

Clinical trials are usually carried out in hospitals, and often take many months or years to collect all the results. They could be funded by a public sector research body, a private foundation or research- funding organisation, or by



a pharmaceutical company. In the later phases, trials are often carried out simultaneously at a number of different study locations – which gives patients an increased chance to take part.

Clinical trials in the EU are regulated by the requirements of the EU clinical trials regulation, which is designed to ensure that no harm comes to the participants in trials and that the outcomes are scientifically validated. The regulation replaced earlier EU requirements which had to be implemented by national legislation; often leading to different interpretations in the different countries. The intention of the clinical trials regulation was to encourage more clinical trials to be conducted in Europe by reducing the differences between the regulatory requirements of different countries.



### Phases

Phase I studies are usually small, involving less than 50 patients and are focused on safety. They aim to identify the best route of administration, any side effects and the best dose to avoid or minimise the unwanted effects.

Phase II trials are conducted on products or treatments that have already successfully completed Phase I, and typically involve up to 300 patients. Larger numbers are needed to make sure that the result is statistically reliable, as different people may respond in different ways to the same treatment, due to their individual genomics. Phase II concentrates on establishing efficacy, whether the product or treatment works, using the dose and route established

in Phase I. Products that are already in use, but are being tested in a new combination or approach, will start with Phase II.

For medications that are intended to treat AL amyloidosis, researchers will need to evaluate whether the disease responds to treatment, whether and by how much the periods of remission can be extended, whether and by how much survival can be prolonged, and whether there is improvement in general quality of life. All these parameters will be compared with the benefit gained from existing treatment, as the overall aim is to find out if the new product or treatment is better than treatments that are already available.

Phase III trials then follow, if a critical proportion of patients show improved benefit from the new treatment compared to existing treatments, and if the side effects are tolerable. Phase III trials can often involve several thousand patients, and they aim to confirm the safety and effectiveness of the new treatment, in comparison to that of 'control' patients given the existing (standard) treatment. Allocation of patients to either the new treatment or the control group is randomised and, if possible, the study is 'blinded' so that the patient does not know which group he or she is in, or 'double-blinded' so that neither the patient nor the doctor knows. These precautions help to avoid any natural inclination in either group to misinterpret the results.

### Inclusion criteria

The protocol for every clinical trial defines its exact purpose, so the researchers must be sure that the participants meet clear criteria so that the trial results concern only what is being tested and could not be explained by some variation between the participants. The criteria for taking part in a specific trial are known as inclusion criteria. They commonly include age, gender, whether the amyloidosis is newly diagnosed or relapsed, what treatment has already been given and whether there are other significant medical conditions.

### Informed consent

Before taking part in a clinical trial, you will be asked to sign a form giving your informed consent. This means having a complete understanding of the purpose of the study, the treatments and tests involved, and possible benefits or risks. While many patients are keen to try a new treatment, others might be more concerned about whether it was any better than what they already have, or about new side effects. Giving informed consent means that you have weighed up all these factors and decided to continue.

## 8.2 Finding out about AL amyloidosis clinical trials

In case you are considering participating in a clinical trial, we recommend that you consult your doctor or healthcare team. They should have access to details of current trials near enough for you to take part, what they are testing and if they are appropriate for your own stage of AL amyloidosis.

The following resources can redirect you to websites that list ongoing or currently recruiting clinical trials in the field of AL amyloidosis:

- [Clinicaltrials.gov](https://clinicaltrials.gov)
- [EU Clinical Trials Register](https://www.eucr.org/)

## 8.3 Novel treatment options in AL amyloidosis

A very important and yet unmet therapeutic goal in AL amyloidosis treatment is the removal of amyloid deposits that are already present in organs at the time of diagnosis, as it could lead to the restoration of organ function. The most common approach under investigation is the use of immunotherapeutic drugs called monoclonal antibodies. These antibodies enable the immune system to recognise the deposits, which enables the body to remove them. For example, two ongoing clinical studies are investigating the efficacy of CAEL-101 in combination with chemotherapy, a monoclonal antibody that binds to AL amyloid deposits; hence it may trigger the immune system-mediated removal of these deposits. Another similar monoclonal antibody, NEOD001 functions in the same way in aiding the body to remove amyloid deposits. However, the phase III clinical trial investigating its efficacy was terminated in 2019 due to no significant therapeutic improvement compared to the control group. That said, a subgroup analysis allowed to identify a possible effect in the advanced stage of the disease. So, a clinical trial using birtamimab (formerly known as NEOD001) is underway.

Since myeloma and AL amyloidosis have a shared pathophysiology (see subsection titled “AL amyloidosis and multiple myeloma”), myeloma treatments may benefit AL amyloidosis patients as well. For example, carfilzomib, the second-generation proteasome inhibitor (see factsheet on [carfilzomib](#)) is being investigated as an alternative treatment option for AL amyloidosis. However, due to possible cardiac toxicity it should be considered only in selected cases of patients with non-severe cardiac damage or isolated peripheral neuropathic involvement. Another agent from the same class, ixazomib is also being

tested, as this medication is known to have a safer side effect profile with regards to cardiac toxicity (see factsheet on [ixazomib](#)). A phase III trial of ixazomib-dexamethasone versus standard of care (TOURMALINE-AL1) was concluded. A chemotherapeutic agent called bendamustine, which is commonly used in non-Hodgkin lymphoma and in myeloma, has also shown efficacy in AL amyloidosis patients. Other options under investigation are: belantamab mafodotin, venetoclax and the applicability of CAR-T cell approach to selected patients with AL amyloidosis.

MPE publishes a conference report after major scientific summits like the American Society of Clinical Oncology (ASCO), the European Hematology Association (EHA) or the American Society of Hematology (ASH); these reports summarise the novel therapeutic options in the field of myeloma and AL amyloidosis. If you are interested in reading about further novel therapeutics under investigation for AL amyloidosis, please visit the “[Conference reports](#)” section of our website.



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## 10. Glossary

- **Alkaline phosphatase (ALP):** a protein (more specifically an enzyme) that is found throughout the body, and plays an essential role in metabolism within the liver and development within the skeleton
- **Anaemia:** a lack of sufficient healthy red blood cells to carry enough oxygen to the body's tissues
- **Amyloid:** A type of wrongly assembled (misfolded) proteins that forms insoluble aggregates, which deposit in tissues and organs
- **Antibodies:** proteins that help our body fight infection; these are made up of large (heavy chain) proteins and small (kappa and lambda) light chain proteins
- **Arrhythmia:** an irregular heartbeat
- **Autologous stem cell transplant (ASCT):** the patient receives an infusion of stem cells derived from themselves
- **Biomarker:** a biological feature/characteristic that can be objectively measured and used to investigate the functioning of certain parts/processes within the body, as well as to monitor if treatments are effective
- **Biopsy:** the removal of a small quantity of tissue from any part of the body to examine it for disease
- **Bone marrow:** the spongy material inside some of the larger bones, which contains stem cells. These stem cells can develop into blood cells
- **Bone marrow aspirate:** a small amount of liquid bone marrow that is removed from inside a bone for the purpose of medical examination. The process of acquiring bone marrow aspirate from a patient is called bone marrow aspiration
- **Bone marrow biopsy:** in a bone marrow biopsy, a portion of solid bone marrow is removed from the patient for medical examination

- **Brain natriuretic peptide (BNP):** a substance produced by the heart to measure its levels in the blood can be used to investigate heart health
- **Chemotherapy:** a drug treatment, which is designed to kill fast-growing cells in the body
- **Cell clone:** a group of identical cells that originate from the same cell
- **Check-up:** a medical examination
- **Diagnosis:** the process of finding out which disease or condition explains a person's symptoms
- **Dysphagia:** difficulty swallowing, taking more time and effort to move food or liquid from the mouth to the stomach
- **Echocardiogram:** a diagnostic test that uses electrodes to check heart rhythm and ultrasound technology to see how blood moves through the heart
- **Enzyme:** a substance (most commonly a protein) that regulates the rate at which chemical reactions proceed in living organisms, without itself being altered in the process. Biological processes that occur within living organisms are fundamentally chemical reactions, and most of these are regulated by enzymes
- **Erythropoietin (EPO):** a hormone that stimulates red blood cell production
- **Fibrils:** a thread- /fibre-like structure made up of proteins
- **Serum free Light Chain (FLC) test** (also found under its commercial name: Freelite® - The Binding Site): light chains are a type of protein produced by plasma cells that link up and form antibodies with heavy chains, another kind of protein produced by plasma cells. Free light chains are light chains that do not link up with heavy chains and circulate in the blood by themselves. An FLC test looks at the amount of such free light chains present, as this can be an indicator of plasma cell abnormalities
- **Heavy chain:** immunoglobulin heavy chains are protein molecules produced by plasma cells that, together with light chain proteins, can assemble into antibodies, hence serving a key role in immune system functioning
- **Immunofixation and electrophoresis:** this test investigates the presence of proteins in the blood or urine. During the electrophoresis phase of the test,

proteins are divided into subgroups according to their electrical charge and size. Next, the proteins can be identified and visualised using antibodies. The results can be observed on a computer monitor, and doctors can identify whether there are too many or too few proteins present in the blood or urine

- **Incidence:** the occurrence of new cases of disease or injury in a population over a specified time period
- **Light chain:** immunoglobulin light chains are protein molecules produced by plasma cells, that, together with heavy chain proteins, can assemble into antibodies, hence serving a key role in immune system functioning
- **Median:** middle value in a list of data/numbers
- **Magnetic resonance imaging (MRI):** a type of diagnostic device that uses strong magnetic fields and radio waves to generate detailed images of the inside of the body
- **N-terminal pro-brain natriuretic peptide (NT-proBNP):** A substance produced by the heart - measuring its levels in the blood can be used to investigate heart health
- **Neutropenia:** the presence of too few neutrophils in the blood
- **Neutrophils:** a type of white blood cell that helps the body fight infection. It is among the first immune cells to respond when pathogens, such as bacteria or viruses, enter the body
- **Peripheral neuropathy:** a condition that results from damage to the nerves located outside of the brain and spinal cord (peripheral nerves). It most commonly causes weakness, numbness and pain in the hands and feet
- **Plasma cells:** a plasma cell is a type of white blood cell, an immune cell that makes large amounts of a specific antibody. Plasma cells develop from B cells that have been activated
- **Platelets** (thrombocytes): a type of blood cell that plays a major role in blood clotting
- **Prevalence:** the proportion of a population that has a specific characteristic (or a given disease) in a given time period

- **Prognosis:** the most likely course of a medical condition
- **Proteins:** essential components of biological organisms. They are made up of amino acids and must assemble into a correct form/shape (folding) to fulfil their biological purposes
- **Proteinuria:** this term refers to increased levels of protein in the urine
- **Red blood cells:** the most common cells in the blood, which serve the function of delivering oxygen to the body's tissues
- **Serum amyloid P component (SAP) scan:** a type of imaging test used in the diagnosis of amyloidosis. In amyloidosis patients, serum amyloid P component coats the surface of affected organs. During the test, a small amount of SAP is injected together with a labelling agent (iodine-123). The injected material localises to the affected organs and thus these can be visualised
- **Thrombocytopenia:** a low blood platelet count, which can cause issues with blood clotting and wound healing
- **Troponin I and troponin T:** proteins found in the muscles of the heart. Normally, they are not present in the blood - their presence in a blood sample indicates heart damage
- **White blood cells:** these cells are a key part of the immune system - they help fight infections and other diseases

# AL amyloidosis

## A Patients' Guide

MYELOMA PATIENTS EUROPE



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