MyelomaUK

Clinical trials and how treatments are developed

Clinical trials and research Infoguide

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Contents

You will find a definition of the terms highlighted in **bold** throughout this booklet in the 'Medical terms explained' section on page 27.

Throughout this Infoguide, the word 'treatment' is used to mean any treatment, from older drugs like chemotherapies, to newer treatments such as monoclonal antibodies. In this Infoguide, 'treatment' also refers to combinations of two or more treatments of any kind that are given together.

'Healthcare team' is used to refer to your hospital team (doctors, nurses and other specialists).

Disclaimer: The information in this Infoguide is not meant to replace the advice of your medical team. They are the best people to ask if you have questions about your individual situation.

This publication is intended for a UK audience. It therefore may not provide relevant or accurate information for a non-UK setting.

Myeloma – an overview

This section explains some key facts about myeloma, including what it is, how it affects patients, and how it is treated. If you are newly diagnosed this section can be a good place to start. If you have been living with myeloma for some time, this information might be familiar but it can still be a useful reminder before reading about specific aspects of myeloma.

Myeloma is a type of cancer arising from **plasma cells** that are normally found in the **bone marrow**. Plasma cells are a type of **white blood cell** which form part of the **immune system**.

Normal plasma cells produce different types of **antibodies** to help fight infection. In myeloma, some of the plasma cells become cancerous (sometimes called **malignant**) and usually release a large amount of a single type of antibody, known as **paraprotein**, which has no useful function. It is often through the measurement of paraprotein that myeloma is diagnosed and monitored.

Sometimes, **myeloma cells** produce only part of the paraprotein, known as **light chains**. These also have no useful function. In other types of myeloma, the myeloma cells only produce small amounts of paraprotein or no paraprotein at all. There are other ways to diagnose and monitor these types of myeloma.

Myeloma affects multiple places in the body where bone marrow is normally active, such as the bones of the spine, pelvis, rib cage and the areas around the shoulders and hips. This is why it is sometimes referred to as 'multiple myeloma'.

Most of the complications and symptoms of myeloma are caused by a buildup of the cancerous myeloma cells in the bone marrow and the presence of paraprotein or light chains in the body.

Common problems in myeloma include bone pain, bone fractures, fatigue, frequent or recurrent infection and kidney damage.

Myeloma is highly treatable in most cases. Treatment is aimed at controlling the disease, relieving the complications and symptoms

it causes, and extending and improving the **quality of life**. Treatment for myeloma is often most effective when two or more drugs, with different but complementary mechanisms of action, are given together.

Myeloma is known as a relapsing and remitting cancer: patients are treated and generally go into **remissions** when their cancer is not active and often is not being treated, followed by **relapses** when the myeloma is active and needs treatment again. Remissions can last for long periods of time, and many patients have a number of remissions and relapses during their lifetime. Although myeloma is not currently curable, the outlook for patients has improved greatly over recent years and is continuing to improve. There are a large number of treatments available, and others are being developed in clinical trials.

The causes of myeloma are not fully understood but it is believed to be caused by an interaction of both genetic and environmental factors.

Key facts

- There are approximately 5,900 people diagnosed with myeloma every year in the UK
- There are over 24,000 people living with myeloma in the UK at any one time
- Myeloma is the third most common type of blood cancer, and accounts for 2% (1 in every 50) of all new cancer cases diagnosed each year
- Although more common in older people, around a quarter (1 in 4) of myeloma patients are diagnosed under the age of 65

Introduction

If you are a myeloma patient, there are many more treatment options available to you now than in the past, even at later lines of treatment. As well as the treatments widely available on the NHS, there are also many promising treatments in the pipeline, being tested in clinical trials.

This Infoguide explains how new treatments for myeloma are developed and how the clinical trial process works. There is practical information about what is involved in taking part in a **clinical trial**, and some things to consider if you are thinking about joining one. There are also sections about how new treatments are authorised for treatment of myeloma, and eventually approved for use on the NHS.

The steps in the process of developing a new treatment are shown in Figures 1 and 2, with links to the pages where each step is described.

For more about myeloma treatments in development, read our Horizons Infosheets at **myeloma.org.uk/library** or visit our drug tracker at **drugs.myeloma.org.uk**

Research into how myeloma cells develop and how the immune system works in myeloma (page 8)

Myeloma treatment target is found (page 8)

Potential treatment is identified that can attack the target (page 8)

Potential treatment is tested in the laboratory for activity and safety

Treatment is formulated into a form that can be given to people, such as an injection or tablet (page 8)

Treatment is tested in clinical trials, initially in small numbers of patients and then in larger numbers (page 10)

Figure 1. How new myeloma treatments are developed, from original discovery to clinical trials

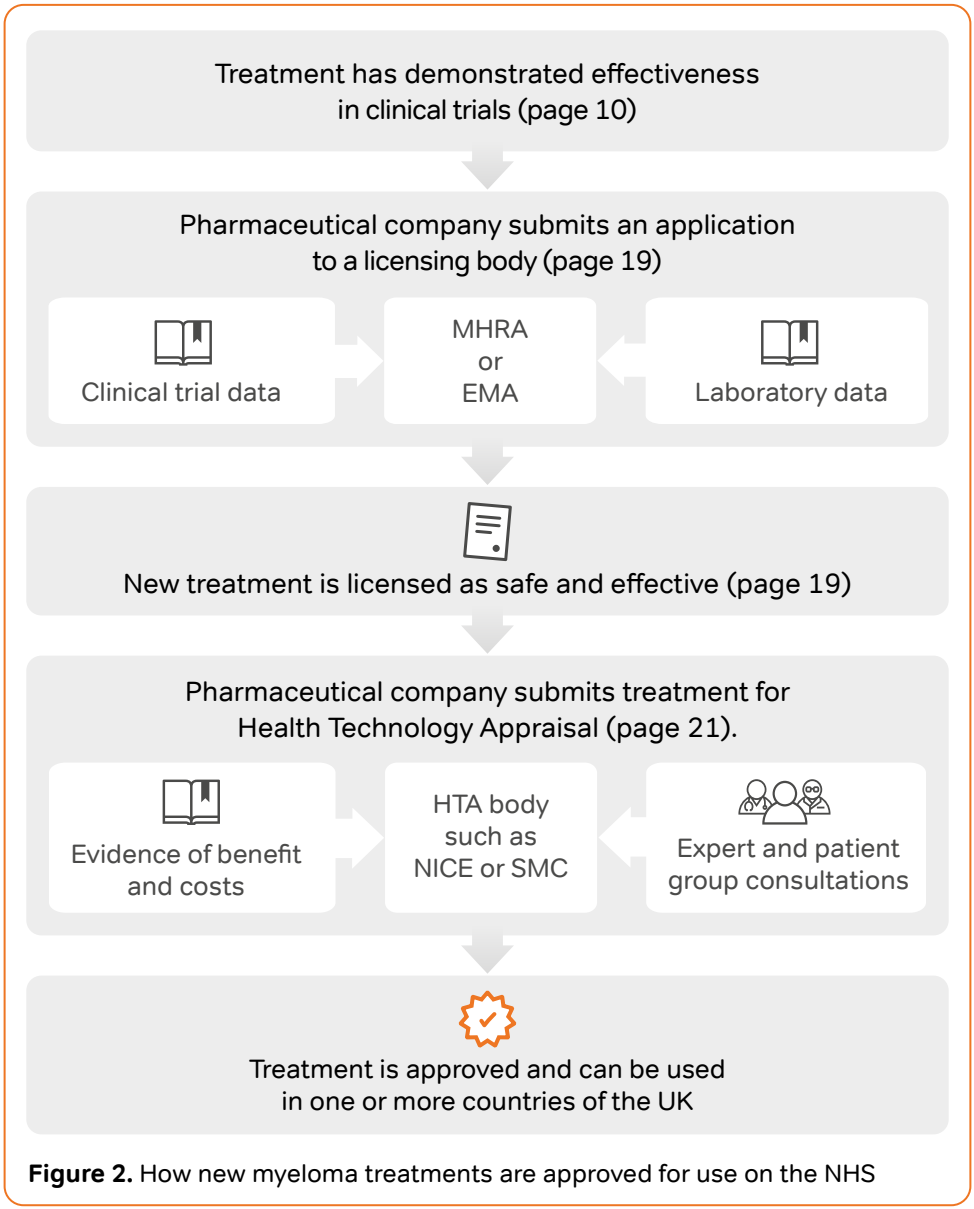

Figure 2. How new myeloma treatments are approved for use on the NHS

How are new treatments developed?

Only a small percentage of treatments make it all the way from the laboratory bench to being approved for use on the NHS. Many potential new treatments are rejected at different points in the process for reasons of safety or effectiveness, and the complete process can take over ten years.

The development of new myeloma treatments takes place over several stages: treatment discovery, laboratory testing, clinical trials, **licensing** and **approval**. These are shown in Figures 1 and 2 (previous pages) and in Table 1 (below).

Stage of development of a myeloma treatment	What happens at this stage
Treatment discovery	Identifying possible new myeloma treatments, based on an understanding of how myeloma develops
Laboratory testing	Potential treatment is tested in the laboratory for activity and safety
Clinical trials	Groups of patients receive the new treatment (or combination of treatments) under carefully controlled conditions. They are closely monitored for tolerability and/or effectiveness of the treatment
Treatment licensing	Treatment (or combination) is licensed as being safe and effective
Treatment approval (Health Technology Assessment)	Treatment (or combination) is approved as being effective and cost-effective for use on the NHS

Table 1. The stages in the development of a new myeloma treatment, from original discovery through to approval for use on the NHS

Treatment discovery

Treatment development starts with treatment discovery. Research is constantly being done into the way myeloma cells work and how they can be attacked. This makes it possible to identify treatment targets (potential ways a treatment could work in myeloma).

In recent years this has involved a lot of research looking at the immune system in myeloma (the group of cells, tissues and proteins that protect the body against infection and disease). A better understanding of how the immune system works in myeloma enables new treatments to be developed that harness the immune system to attack myeloma cells.

After the treatment discovery phase, research is then carried out into the effects of a treatment (or combination) on myeloma cells in the laboratory.

After safety and effectiveness testing in the laboratory, successful treatments go through a process of **formulation**. This means that the active drug is mixed with other ingredients to produce a form that can be given to patients (such as an **intravenous** infusion or an **oral** tablet or capsule).

The treatment can then be tested in people, in clinical trials. The next section (page 10) explains more about clinical trials.

Treatment names

Treatments initially have code names or numbers used by the scientists working on them.

If a treatment progresses further it will get an official name called a **generic name**. This gives some information about the type of treatment. For example, **bortezomib**, **carfilzomib** and **ixazomib** have names ending in “zomib”, because they are all **proteasome inhibitors**.

Once a treatment is nearer to being licensed for sale, it will be given a **brand name** by the pharmaceutical company developing it. For example, bortezomib is sold under the brand name of Velcade®. Some treatments have more than one brand name (if

they are sold in different countries, or if more than one pharmaceutical company is selling them).

Patents

When a pharmaceutical company develops a treatment, they apply for a **patent** for it. This means they are the only company able to make this treatment. Patents run out after a certain amount of time, after which other companies are able to make the treatment. The new versions of the treatment are known as **generic drugs**, and function in the same way as the original treatment. A generic treatment can normally be purchased much more cheaply and competitively by the NHS. Usually, this means more combinations involving the treatment may be developed, if they are shown to be effective.

Clinical trials

A clinical trial of a myeloma treatment involves a group of patients receiving the treatment or combination under carefully controlled conditions. During the trial, they are closely monitored for the tolerability and/or effectiveness of the treatment.

The information collected during the trial is analysed by trained researchers. The results are used to decide whether a new treatment progresses to the next stage of clinical trials. Eventually, the trial results are used by regulatory authorities to decide whether the treatment should be licensed for use in patients.

A new treatment for myeloma will go through different phases of clinical trials, with different aims and designs. The usual types of clinical trial at each phase are described below and summarised in Figure 3.

Although this Infoguide focuses on treatment development, clinical trials don't just test new treatments. They can also be used to test differences in all elements of treatment and care, including diet, exercise, patient support, sleep and healthcare services.

Phase 1	Phase 2	Phase 3
		
10s of people or fewer	**20–150 people**	**100s or 1,000s of people**
Safety	Confirmation of safety	Confirmation of safety and effectiveness
Best dosage	First indication of effectiveness	How treatment compares to current treatment(s)

Figure 3. The phases of clinical trials, showing typical numbers of patients included, and what are the aims at each phase.

Phase 1

The main priority of Phase 1 trials is to investigate how well tolerated a new treatment is when given to patients. Trials that are 'first in human' with a new type of treatment may start with extremely low doses of the treatment given to very small numbers of patients, gradually increasing the dose in more patients if no safety concerns are raised. Other Phase 1 trials will start at doses that are near to those likely to be active. The aim is to find an active but well-tolerated dose that will be used in the next phase.

Phase 1 trials may produce some information about effectiveness of the treatment, but this is not the main aim.

Phase 1 trials may also look at how fast the treatment is taken up in the body, how long it stays in the body, and how it is removed (for example filtered out by the kidneys). This is called the **pharmacokinetics** of the treatment. This information will help determine the best dosing schedule for the new treatment.

Other Phase 1 trials may be looking at combination treatments, where a new treatment is combined with a standard myeloma treatment to see how well-tolerated the combination is.

Phase 2

Phase 2 clinical trials are often larger than Phase 1. The aim is to get information about effectiveness, and more information about tolerability and pharmacokinetics. A dose may be used that has been shown to be active and well-tolerated in Phase 1, or a range of different doses may be given to different patients to check for the most effective dose.

Some Phase 2 clinical trials compare a new treatment with a standard myeloma treatment.

Phase 3

Phase 3 clinical trials are generally much larger. The purpose is to produce stronger evidence of the effectiveness of the new treatment. This is because larger trials can produce more reliable **statistics**.

Phase 3 trials are usually **comparative**, which means they compare different treatments. Groups of patients are given different treatments (called **arms** of a trial). Often the new treatment is compared with an existing one, or combinations of the new treatment with different existing treatments are compared.

Patients are assigned to the different treatment groups by a process called **randomisation**. This means that which treatment they are given is decided by chance. Randomisation is done to help avoid bias in the study, and to ensure that there is an equal mix of patients with different characteristics (such as age, gender and other factors) in each group.

No matter which group you are put into on a clinical trial, you will receive treatment for your myeloma.

Taking part in a clinical trial

Many myeloma patients have questions about taking part in clinical trials. Your healthcare team may have mentioned that a clinical trial may be appropriate for you. In some cases, if you have limited treatment options available, a clinical trial may enable you to access a new treatment that is being developed. This section gives some information about the practicalities of taking part in clinical trials.

A clinical trial is part of your clinical care, and a trial will only be suggested for you if it is in your own best interests. Your own healthcare team will discuss the trial with whoever is co-ordinating it. There will be a doctor who is responsible for running the trial in the hospital, and in many cases a research nurse will liaise between the people involved.

How can I find out about clinical trials?

Your doctor may discuss with you the possibility of taking part in a clinical trial. This may be when you are newly diagnosed or starting to relapse.

You can also find out about clinical trials from the Myeloma UK Trial Finder (**trials.myeloma.org.uk**), or from the Myeloma Infoline and Ask the Nurse service.

What factors affect whether I take part in a clinical trial?

It is important to understand that not every patient is suitable for every new treatment, or for a particular clinical trial. To be enrolled on a clinical trial, patients have to meet certain conditions (known as **eligibility criteria**) for the trial. These may include:

- Age
- Number of previous lines of treatment, and what those were
- Medical history (such as kidney function)

These criteria are to protect patients in the trial – for example, to ensure that patients with very poor kidney function are not given a treatment that could harm them. The criteria are also important in how the results of the clinical trial will be analysed.

There are also practical factors. Each trial will have one or more centres (hospitals taking part in the trial). Therefore, you would need to be able to get to one of the hospitals taking part in the trial, and there will often be extra monitoring visits during the trial.

If there is more than one trial potentially available to you, your haematologist will discuss which trial is best for you, depending on your own best interests and your preferences.

Will my clinical care be different if I am in a clinical trial?

Much of your care will be just the same whether or not you are part of a clinical trial. You may have more frequent assessments such as scans, bone marrow tests, blood and urine tests.

Protection of patients in clinical trials

Clinical trials are run according to a strict plan called a **protocol**. The protocol must be agreed by various bodies, including **ethics committees**, before the trial can go ahead. This is to protect the rights and safety of the patients taking part.

Taking part in clinical trials is voluntary. You can withdraw at any time, and if you do so this won't have any detriment on your care.

All patient-related information collected in the trial is kept strictly confidential, and patients will not be identified in reports or publications about the trial.

Making the decision about taking part in a clinical trial

If you are considering taking part in a clinical trial, your healthcare team will discuss in detail the possible benefits and risks for you. They will give you the information you need so you can make an informed decision about whether to take part (called **informed consent**).

It may also help to talk through your options with a Myeloma Information Specialist – call **0800 980 3332** or email **AsktheNurse@myeloma.org.uk**

Things to consider about taking part in a clinical trial include:

- Will you have to travel to a different hospital to receive your treatment?
- If so, can you reclaim travel costs? Ask what arrangements are available locally
- Will the treatment be for a certain number of cycles, or will it be given until it no longer benefits you?
- Will the trial involve extra tests and investigations?
- How long will the trial follow-up period last?
- Can you continue with the treatment after the trial is finished, if it is benefitting you?
- What treatment will you be offered if you decide not to take part in the trial, or if you have to stop taking the trial treatment(s)?

Clinical trials can provide you with the opportunity to access new treatments not yet available on the NHS. Patient participation in clinical trials is vital in making new treatments available more widely.

What happens after a clinical trial?

You will be followed up after the main trial period, often for a long time – for example to find out how long it is before your myeloma starts to come back.

In the UK, clinical trials do not count as lines of treatment, meaning that patients would re-enter the treatment pathway where they left off, but you should confirm this with your medical team before starting on a trial.

Although it shouldn't affect your lines of treatment, the treatment you receive in the trial may impact what treatments you could have in the future. Some treatments have specific eligibility requirements that depend on your treatment history, including treatment received in a clinical trial.

For an up-to-date list of UK clinical trials in myeloma, visit the Myeloma Trial Finder at **trials.myeloma.org.uk**
To find out more about specific treatments in development, read our Horizons Infosheets at **myeloma.org.uk/library**

Myeloma research

Research into myeloma (like that in other treatment areas) is highly collaborative, with researchers around the world communicating about the research they have done and what they are planning. This section explains more about these wider aspects of myeloma research, and how clinical trial results are interpreted.

Who does myeloma research?

Research into myeloma treatments takes place around the world, and is often done in collaboration between researchers in different countries. Many clinical trials are what is called **multicentre**, meaning that patients at a number of different hospitals (often including different countries) are taking part in the clinical trial.

There is much communication between researchers doing different clinical trials, which helps to speed progress and to make sure research is not duplicated. Communication is through scientific journals, national and international myeloma conferences, and groups such as the International Myeloma Working Group (IMWG), the UK Myeloma Society (UKMS) and the UK Myeloma Research Alliance (UKMRA).

The UKMRA is the national organisation in the UK that oversees patient research in myeloma and related conditions. Myeloma UK funds research through the UKMRA-Myeloma UK-CARP (Concept and Access Research Programme).

Read more about Myeloma UK's involvement in research at **myeloma.org.uk/research-and-impact/our-research**

Interpreting clinical trial results

The results of clinical trials are an important part of the process of developing new myeloma treatments. The next two pages explain more about how clinical trial results are interpreted.

How is effectiveness measured?

The effectiveness of myeloma treatments is measured in different ways in clinical trials, and not all these are considered equal.

The ultimate goal for any myeloma treatment is to extend life and as a result, the main measure for effectiveness is how long patients live after receiving the treatment (**overall survival**).

Overall survival data can take years to generate, especially when developing new treatments for newly diagnosed patients. Therefore, other measures of effectiveness are often used as an indication of how well treatments work, particularly in earlier phase clinical trials.

One of these measures is **response rate**. This is a measure of the decrease in paraprotein and myeloma cell levels following treatment. Response is scored at different levels (such as complete response and partial response). These levels of response are shown in Table 2. Clinical trials usually report 'overall response rate', which is the percentage of patients who have a partial response or better.

Response rate	Summary of how the response is defined
Stringent complete response (sCR)	No detectable paraprotein No detectable myeloma cells in the bone marrow
Complete response (CR)	No detectable paraprotein <5% myeloma cells in the bone marrow
Very good partial response (VGPR)	>90% reduction in paraprotein
Partial response (PR)	>50% reduction in paraprotein
Minor response (MR)	<50% reduction in paraprotein
Stable disease (SD)	No change in paraprotein levels
Progressive disease (PD)	Increase in paraprotein levels

Table 2. How different levels of response are defined in clinical trials

Response rate gives researchers an early indication of how well the new treatment is working.

Another way of measuring the depth of response is **minimal residual disease (MRD)**. MRD is the very small number of myeloma cells remaining after successful treatment, which can be measured (usually in bone marrow samples) using very sensitive analysis techniques. After treatment, patients are defined as 'MRD negative' or 'MRD positive':

- 'MRD negative' means the level of myeloma cells is too low to be detected
- 'MRD positive' means myeloma cells can still be detected by the analysis techniques

MRD is a relatively new measure, and is so far only really used in clinical trials. It is hoped that MRD could become a standard measure of response in clinical trials, and that it could predict the effect of treatments on overall survival.

Another measure of response used in clinical trials is called **progression-free survival**. This is the length of time before a person's myeloma starts coming back.

How can different clinical trials be compared?

It is not possible to compare the results of different treatments directly across separate clinical trials. This is because the trials were done at different times, and the patients in the trials may not be directly comparable (for example, there may have been different eligibility criteria). For this reason, it is important that part of the process of developing a new treatment involves direct comparisons of treatments. A new treatment in development will be compared with an established treatment.

Larger clinical trials (Phase 3) are usually of this type (called comparative trials). The treatment groups can be compared because the patients in the groups have the same characteristics (such as age and stage of myeloma), and patients are allocated to the treatments randomly.

Treatment licensing

Before a treatment (or combination) can be widely used, it must first be licensed as safe and effective. Read this section for more about what treatment licensing involves, and who licenses treatments in the UK.

The results of clinical trials and other studies are used to decide whether a treatment should be licensed. The licence (called a **marketing authorisation**) will specify the patient groups the treatment is for (for example newly diagnosed patients) and how the treatment is given (for example in a particular combination with other treatments). These will be based on the evidence gained from clinical trials.

Once the treatment has been licensed, the pharmaceutical company that developed it has the authority to sell it, and doctors can prescribe it. However, at this stage it is not guaranteed to be funded by the NHS.

Licensing specifies the way the treatment is used, for example:

- What it is used for (in this case, myeloma)
- The recommended dose
- Whether it is given in combination with other treatments
- How the treatment is given – for example as a tablet, intravenous infusion (into a vein) or subcutaneous injection (under the skin)

Who licenses treatments in the UK?

The procedures for licensing treatments in the UK changed after the UK's departure from the European Union (Brexit), and they are still in transition. There are several possible routes to a treatment or combination being licensed in the UK.

The **Medicines and Healthcare products Regulatory Agency (MHRA)** licenses treatments in the UK, and is able to take into account licensing decisions made by the European Commission, which licenses treatments based on the recommendations of the **European Medicines Agency (EMA)**. In Northern Ireland, treatments can be licensed via the EMA or via MHRA licensing. From 2025, it will only be the MHRA that can license new treatments for use in Northern Ireland.

Conditional licensing

In some cases, new treatments may be given a conditional licence (called a **conditional marketing authorisation**). This means that more evidence about the treatment is needed (from additional, or larger, clinical trials). The treatment is licensed ahead of this, because it addresses an unmet need for patients who have limited options for treatments.

Approving treatments for use on the NHS

After a treatment has been licensed (see previous section), the final stage is approval for use on the National Health Service (NHS) in the UK. Treatment approval is different from licensing. It looks at the benefits of the newly licensed treatment or combination, and compares these with existing treatments already in use on the NHS.

The approval process looks at these questions:

- How well does the new treatment or combination work?
- Is the new treatment or combination good value for money?
- How well does it work in relation to its cost to the NHS? This part of the appraisal will include information submitted by the pharmaceutical company about the costs and value of the treatment or combination

The treatment approval process is called **Health Technology Assessment (HTA)** or technology appraisal.

Treatments for myeloma are approved for use on their own or in specific combinations. The approval will normally be for use at specific treatment lines. These decisions are based on the evidence from clinical trials, which are used to help determine where in the treatment pathway a treatment or combination would provide most benefit to patients.

Although value for money (cost-effectiveness) is always a consideration in the approval process, the approach will be flexible and will depend on the type of medical condition. In more serious conditions such as myeloma, more weight will be given to health benefits, to increase access to new treatments and combinations.

A licensed treatment that has not been approved for use on the NHS may be available to patients through private healthcare or other routes (see Accessing treatments before approval, page 24).

Who approves treatments in the UK?

Treatment approval is done by different organisations (called Health Technology Assessment (HTA) bodies) in different parts of the UK:

- **England**: The **National Institute for Health and Care Excellence (NICE)** decides which treatments and combinations are available for use on the NHS in England. When treatments and combinations have been approved by NICE, the NHS in England is legally obliged to fund them
- **Scotland**: The **Scottish Medicines Consortium (SMC)** decides which treatments and combinations are available for use on the NHS in Scotland. Its decisions are separate from those made by NICE. Health Boards in Scotland are expected to make treatments approved by the SMC available. There is also a new body called the National Cancer Medicines Advisory Group (NCMAG), which can advise the NHS in Scotland on use of treatments outside their product licences for cancer patients
- **Wales**: The **All Wales Medicines Strategy Group (AWMSG)** decides which treatments and combinations are available on the NHS in Wales. In general, they choose to follow NICE decisions. Individual health boards may decide to approve a treatment that has not been approved for the whole of Wales
- **Northern Ireland**: The Department of Health makes decisions about health and social care. They usually choose to follow NICE or SMC decisions

The manufacturing pharmaceutical company is responsible for submitting an application to the approval bodies. NICE and the SMC have to publish information on their websites about approval decisions they make, and the reasons for them.

Funding schemes for treatments in myeloma

The **Cancer Drugs Fund (CDF)** is a source of funding for cancer treatments in England. It aims to provide cancer patients in England with faster access to the most promising new treatments, before they are fully approved by NICE for use on the NHS. A treatment may be approved for use within the CDF for a set time period, while more evidence is being collected. Treatments approved in this way are normally made available in Wales and Northern Ireland as well.

The **New Medicines Fund** in Scotland helps health boards to fund the cost of treatments for patients with rare diseases such as myeloma, or who are nearing the end of life.

The patient's voice in treatment approval

Patient involvement is key in the treatment approval process. Patients, and patient organisations, have opportunities to contribute to decision-making by the treatment approval bodies. Myeloma UK works with the treatment approval bodies to make sure that the voice of myeloma patients is heard, and we include evidence from patients in our submissions to them. We also work collaboratively in partnerships such as Cancer52 (**cancer52.org.uk**) and the Blood Cancer Alliance (**bloodcanceralliance.org**).

Find out more about our work in improving access to treatment on our website at **myeloma.org.uk/advocacy**

Accessing treatments before approval

When treatments are not yet approved for use on the NHS, patients can sometimes access them through a different route. The first step is to talk to your consultant, and find out whether any of these routes is open to you.

Clinical trials

You may be able to take part in a clinical trial of an unlicensed treatment. This is explained in the earlier sections of this Infoguide.

Expanded access (compassionate use) schemes

Patients can sometimes access new treatments in development through **expanded access (compassionate use) schemes**. These schemes are sometimes set up by pharmaceutical companies to give patients access to new treatments that are still in development. They are only for patients who have no other suitable treatment options and who cannot join a clinical trial. Requests for expanded access can only be made by a haematologist.

Individual funding requests (IFRs)

In special circumstances, a haematologist may make an **individual funding request (IFR)** for a treatment not approved for use on the NHS.

Your haematologist can apply for an IFR if they think your clinical situation is different from that of other myeloma patients, or that you have a higher chance of benefiting from the treatment than other myeloma patients. These applications take time and are not always successful.

Private healthcare

If a treatment is licensed by the MHRA or EMA, but not approved for use on the NHS, patients may be able to access it through private healthcare. This may be self-funded or funded through health insurance, but it is not available at every hospital.

Private treatments are not necessarily better for you than those available through the NHS. Therefore, it is important that you discuss your options with your current haematologist in the first place. If appropriate, they may then refer you to a private haematologist.

Private healthcare for myeloma can be a very expensive option. As well as the treatment itself, which may be expensive, you would also need to pay privately for any other treatments it is used in combination with, and for any supportive treatment and care.

After a treatment is approved

After a treatment has been approved for use on the NHS, many more patients will be treated with it than at the clinical trial stage. This means there are opportunities to look further at its effectiveness and safety.

Examples are:

- **'Real-world'** data can be collected – this is evidence about routine use of the treatment in patients in the clinic. Unlike in clinical trials, where patients are carefully selected for the trial, patients in the 'real world' are likely to have a wider range of medical histories
- Ongoing data about suspected **side effects** of treatments is collected. This is called **drug surveillance**, and the UK scheme is called the **Yellow Card scheme** (yellowcard.mhra.gov.uk). Although healthcare professionals most often do this reporting, anyone can report a suspected side effect. All the reports help to build up a more accurate picture of the side effect profile of the treatment. Rare side effects (ones occurring in 1 in 10,000 patients treated) may only become apparent once a treatment is in widespread use
- New clinical trials (called Phase 4 trials) may also be done. These may be done:
  - To look at the new treatment in combinations not previously tested at Phase 3
  - To get information from longer-term trials about effectiveness and tolerability
  - To get information about use of the treatment in specific patient groups such as elderly patients or those with kidney problems

Medical terms explained

All Wales Medicines Strategy Group (AWMSG): A public body that is responsible for deciding which treatments are made available for use on the NHS in Wales.

Antibodies (immunoglobulins): Proteins found in the blood which are produced by cells of the immune system, called plasma cells. Their function is to bind to substances in the body that are recognised as foreign, such as bacteria and viruses, enabling other cells of the immune system to destroy and remove them.

Approval (of a treatment): The process of approving a treatment for use on the NHS. It is also called Health Technology Assessment.

Arm (of a clinical trial): Group of patients in a comparative clinical trial who are all receiving the same treatment.

Bone marrow: The soft, spongy tissue in the centre of bones that produces blood cells.

Bortezomib: A proteasome inhibitor drug which is given as a subcutaneous injection.

Brand name: The name used by a pharmaceutical company for a drug once it is licensed for sale (for example, Velcade® is the brand name for bortezomib).

Cancer Drugs Fund (CDF): A source of funding that aims to provide cancer patients in England with faster access to the most promising new treatments, before they are fully approved by NICE for use on the NHS.

Carfilzomib (Kyprolis®): A proteasome inhibitor drug which is given as an intravenous infusion.

Clinical trial: A research study of new or existing treatment or care that involves patients. Trials may be designed to find better ways to prevent, detect, diagnose, or treat a condition or to answer specific scientific questions.

Comparative trial: A clinical trial comparing two or more different treatments.

Conditional marketing authorisation: A licence for a treatment where comprehensive clinical data is not yet fully available. It is granted for treatments that address an unmet need, for patients who have limited treatment options. Also known as a conditional licence.

Drug surveillance: Monitoring suspected side effects of treatments, after they are licensed and in widespread use.

Eligibility criteria: Specific conditions that have to be met to take part in a particular clinical trial (for example age or number of previous treatments).

Ethics committee: An independent group of people that reviews clinical trial proposals to assess whether they are ethical. They look at the protocol, the aims, design and organisation of the clinical trial, and the safety and wellbeing of patients taking part. They include members of the public and experts.

European Medicines Agency (EMA): The body that makes recommendations to the European Commission on licensing of treatments in the European Union.

Expanded access (compassionate use) schemes: Schemes sometimes set up by pharmaceutical companies to give patients access to new treatments that are still in development.

Formulation: The process by which a drug is mixed with other ingredients to produce a form that can be given to patients (such as an intravenous infusion or an oral tablet or capsule).

Generic drug: A drug that contains the same chemical substances as a drug that was originally developed and protected by a patent. Generic drugs can be made and sold after the patent for the original drug has run out.

Generic name: The official name of a drug (for example bortezomib).

Health Technology Assessment (HTA): Process by which a treatment is assessed before being approved for use on the NHS. The HTA process includes assessment of effectiveness, and of costs and benefits. Also known as treatment approval or technology appraisal. HTA is undertaken by public bodies such as the National Institute for Health and Care Excellence (NICE).

Immune system: The complex group of cells, tissues and proteins (including antibodies), that protect the body against infection and disease.

Individual funding request (IFR): A request made by a doctor for funding to treat an individual patient, using a treatment not approved for use on the NHS.

Informed consent: The process of making an informed decision about whether to take part in a clinical trial. The clinical trial is explained and information is given in writing, and the person can ask questions and take time to think about whether to take part.

Intravenous (IV): Into a vein.

Ixazomib (Ninlaro®): A proteasome inhibitor drug which is given orally.

Licensing (of a treatment): The process of granting a marketing authorisation (previously called a product licence).

Light chains: Part of an antibody (or immunoglobulin). An antibody is made up of two heavy chains and two light chains. There are two types of light chain, kappa and lambda.

Malignant: A term for cancerous cells which have the ability to spread.

Marketing authorisation: The authorisation to sell a treatment. It was previously called the product licence, and is granted based on safety and effectiveness.

Medicines and Healthcare products Regulatory Agency (MHRA): The body which grants marketing authorisations (licences) for treatments in the UK.

Minimal residual disease (MRD): The very small number of myeloma cells that survive in the bone marrow after successful treatment, which can be detected using highly sensitive analysis.

Monoclonal antibody: A type of synthetic drug that mimics the actions of antibodies.

Multicentre (clinical trial): A clinical trial taking place at a number of different hospitals. It may be in more than one different country.

Myeloma cells: The abnormal plasma cells that occur in myeloma.

National Institute for Health and Care Excellence (NICE): A public body responsible for assessing the clinical evidence and cost-effectiveness of new treatments for use on the NHS in England.

New Medicines Fund: A fund that helps health boards in Scotland to fund the cost of treatments for patients with rare diseases such as myeloma, or who are nearing the end of life.

Oral: By mouth.

Overall survival: How long patients live.

Paraprotein: An abnormal antibody (immunoglobulin) produced in myeloma. Measurements of paraprotein in the blood can be used to diagnose and monitor the disease. Also known as M protein.

Patent: The legal right to make or sell an invention (such as a myeloma treatment) for a particular number of years.

Pharmacokinetics: The movement of a drug within the body (including how fast it is taken up, how long it stays in the body, and how it is broken down and removed).

Plasma cells: A type of white blood cell that produces antibodies (immunoglobulins) to fight infection.

Plateau: A period of time when the myeloma, and the paraprotein level, is relatively stable. Often referred to as stable disease.

Progression-free survival: The length of time before a person's myeloma starts to come back.

Proteasome inhibitor: A type of drug which interferes with the normal functioning of a part of the cell called the proteasome, which is involved in the removal, breakdown and recycling of damaged or no longer needed proteins.

Protocol: The document that describes all the aspects of a clinical trial (including its purpose, design, methods, how the trial will be organised, who is responsible for running the trial, and how the results will be analysed).

Quality of life: A term that refers to a person's level of comfort, enjoyment, and ability to pursue daily activities. It is a measure of an overall sense of wellbeing.

Randomisation: The process by which patients entering a clinical trial are randomly allocated to one of the treatment groups.

Real-world data: Evidence about routine use of a treatment, collected in hospitals or general practice.

Relapse: The point where disease returns or becomes more active after a period of remission or plateau.

Remission: The period following treatment when myeloma cells and paraprotein are no longer detectable, and there are no clinical symptoms of myeloma.

Response rate: A measure of the decrease in paraprotein and myeloma cell levels following treatment. It is used in clinical trials to measure the effectiveness of treatment.

Scottish Medicines Consortium (SMC): A public body that is responsible for assessing the clinical evidence and cost-effectiveness of new treatments for use on the NHS in Scotland.

Side effects: The undesired effects caused by a drug or treatment, for example fatigue or nausea.

Statistics: The science of collecting and interpreting data (measurements). In a comparative clinical trial, for example, statistics would be used to determine how likely it is that a difference seen between the effectiveness of two treatments is just the result of chance.

Treatment target: A term used to describe a potential way that a treatment could work in myeloma. For example, a protein found on the surface of myeloma cells (the treatment target) could be attacked by a monoclonal antibody drug.

White blood cells: A type of blood cell involved in the body's immune system, which help to fight infection and disease.

Yellow Card Scheme: UK scheme to collect and monitor data about suspected side effects of treatments in general use.

Notes

Useful organisations

Carers UK carersuk.org
0808 808 7777
Provides advice, information and support for carers.

Citizens Advice citizensadvice.org.uk
www.adviceni.net
England: **03444 111 444** Wales: **03444 77 20 20**
Scotland: **0800 028 1456** Northern Ireland: **0800 915 4604**
Offers advice about debt and consumer issues, benefits, housing, legal matters and employment.

Macmillan Cancer Support macmillan.org.uk
0808 808 0000
Provides practical, medical and financial information and support to all cancer patients and their carers.

Maggie's www.maggies.org
0300 123 1801
Provides free practical, emotional and social support to people with cancer and their family and friends.

Mind mind.org.uk
0300 123 3393
Provides advice and support to empower anyone experiencing mental health problems.

NHS 111 Service nhs.uk/111
111
Call 111 when you need medical advice fast but it's not a 999 emergency. NHS 111 is available 24 hours a day, 365 days a year.

Samaritans samaritans.org
116 123
Listening and support free, 24 hours a day, to anyone who's struggling to cope.

We're here for everything a diagnosis of myeloma brings

Visit **myeloma.org.uk**, a one-stop-shop for information on myeloma; with videos, news and articles to help you keep up to date and live well with myeloma.

Call our **Myeloma Infoline** on **0800 980 3332** for practical advice, emotional support and a listening ear.

Get answers to your questions by emailing our Myeloma Information Specialists at **AskTheNurse@myeloma.org.uk**

Order or download our **information booklets**, which cover all aspects of myeloma - call **0800 980 3332** or visit **myeloma.org.uk/publications**

Learn about myeloma from experts and meet other patients at our **Infodays** and **Digital Infoday Sessions**.

Join a **Myeloma Support Group** to meet other people living with myeloma face to face or online.

Get matched up with a trained **Peer Buddy** for one-to-one support from someone with direct experience of myeloma.

Chat and share experiences with others affected by myeloma, including our peer volunteers, on the **Discussion Forum.**

We need your help

Thanks to our generous supporters we are able to provide information and support to patients and their families, as well as fund vital research that will help patients live longer and with a better quality of life.

Myeloma UK receives no government funding. We rely on fundraising activities and donations.

You can support Myeloma UK by:

- **Making a single donation or setting up a Direct Debit**
  Online at **myeloma.org.uk/donate**
  Over the phone **0131 230 0429**
  Or by posting a cheque payable to **Myeloma UK** to:
  Myeloma UK, 22 Logie Mill, Beaverbank Business Park, Edinburgh, EH7 4HG
- **Fundraising** – fundraising is a positive way of making a difference and every pound raised helps. As myeloma is a rare, relatively unknown cancer, fundraising is also a great way to raise awareness
- **Leaving a gift in your will** – legacies are an important source of income for Myeloma UK and help us to continue providing practical support and advice to myeloma patients and their families. They also help us to undertake research into the causes of myeloma and investigate new treatments

However you decide to raise funds, our Fundraising Team is here to support you. Contact us on **0131 230 0429** or email **fundraising@myeloma.org.uk**

Nobody ever forgets the moment they are diagnosed with myeloma. Myeloma UK advances the discovery of effective treatments, with the aim of finding a cure. That is what patients want, it's what they deserve and it's what we do.

Judy Dewinter – President, Myeloma UK

We appreciate your feedback. Please fill in a short online survey about our patient information at **myeloma.org.uk/pifeedback** or email any comments to **patientinfo@myeloma.org.uk**

For a list of references used to develop our resources, visit **myeloma.org.uk/references**

Clinical trials and research Infoguide:
Clinical trials and how treatments are developed

MyelomaUK

We're here for everything a diagnosis of myeloma brings

Get in touch to find out more about how we can support you

Call the Myeloma Infoline on
0800 980 3332

Email Ask the Nurse at
AskTheNurse@myeloma.org.uk

Visit our website at
myeloma.org.uk

Trusted Information Creator
Patient Information Forum

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