Myeloma XI

Myeloma Infoguide Series

www.myeloma.org.uk
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Disclaimer
The information in this guide 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.
Introduction

This Infoguide is written for myeloma patients. It may also be helpful for their families and friends. It provides information about the Myeloma XI clinical trial, what it involves and what to expect.

Some of the more technical words appear in bold the first time they are used and are described in the Medical terms explained section on page 57.

This Infoguide aims to:

- Provide information about the Myeloma XI trial and explain why it is taking place
- Describe what is involved if patients decide to take part in the trial
- Answer some of the more common questions about the trial
- Help patients make an informed decision on whether to take part in the trial

This Infoguide does not replace the Myeloma XI trial’s patient information. It is only intended to provide general information to help explain the trial. Anyone considering taking part in the trial should consult their doctor to obtain the trial’s patient information.

Version 6 protocol

At the end of 2013 a new protocol was introduced for the Myeloma XI clinical trial – this is known as version 6. All information for version 6 will be clearly marked in a box like this. It is very important that you know which protocol you are on. If you are not sure ask your doctor or nurse.
Myeloma UK also provides a range of other Infoguides and Infosheets which cover all aspects of the treatment and management of myeloma. A list of the available publications can be found on pages 73 – 74.

For a more general overview of what myeloma is and the commonly used treatments and how to cope with living with myeloma, see:

- *Myeloma – Your Essential Guide* and
- *Living with Myeloma – Your Essential Guide*

To find out more about clinical trials see:

- *Clinical Studies Infoguide*

To order free copies call the **Myeloma Infoline on 0800 980 3332**. This information is also available to download at [www.myeloma.org.uk](http://www.myeloma.org.uk)

To talk to one of our Myeloma Information Specialists about any aspect of myeloma, call the **Myeloma Infoline on 0800 980 3332** from Ireland. The Myeloma Infoline is open from Monday to Friday, 9am to 5pm and is free to phone from anywhere in the UK. From outside the UK, call +44 (0)131 557 9988 (charged at normal rate). Information and support about myeloma is available around the clock at [www.myeloma.org.uk](http://www.myeloma.org.uk)
What are clinical trials?

Clinical trials are planned research investigations in which patients take part. They are designed to test new drugs or new combinations of current treatments, or to compare different ways of using current treatments. Their purpose is to find out whether or not the new drug, new combination or treatment approach is of greater benefit to patients than the current standard treatment.

Clinical trials are run according to a strict trial plan called a protocol. The protocol must be inspected and approved by various regulatory bodies, including an ethics committee, before the trial can start. These processes are in place to protect the rights, dignity and safety of those taking part.

Patients involved in a clinical trial are closely monitored to determine the safety, efficacy and effectiveness of their treatment. The information collected during the course of the trial is gathered and analysed by trained researchers. As a result of this analysis, protocols for clinical trials can be updated whilst the trial is underway. If this happens, usually patients already in the trial will continue treatment on the protocol they started on.

The final results of the trial help determine which of the treatments being tested is best. Where relevant, the new treatment will be put forward for further testing or, if there is enough evidence, become the standard treatment. Clinical trials are therefore important for developing better ways of treating patients.

Not all patients will be suitable for a clinical trial. Doctors and researchers only ask patients who are suitable for the treatments being studied to take part. Each trial will have eligibility criteria – a set of requirements for the trial that patients must meet. These criteria are very important and help to protect the safety of patients to ensure they are not exposed to any unnecessary risks and to ensure that the relevant population of patients take part so that the clinical questions can be answered under the appropriate setting.

Taking part in a clinical trial is entirely voluntary. It is always up to patients to decide whether they want to take part in a clinical trial or not. Anyone considering taking part in a clinical trial will be provided with all of the information about the trial and the support needed to enable them to make a decision.
If patients decide to take part in a clinical trial, they will be asked to sign an Informed Consent Form. For more information on informed consent, see page 21 of this Infoguide.

Most clinical trials have two or more treatment pathways. Patients who take part in a clinical trial are assigned to a specific treatment pathway by a process called randomisation.

This means that a computer system will decide by chance which treatment pathway the patient will follow. The computer has no information about the patient and the likelihood of them being placed in each treatment group is equal. Neither the patient nor their doctor can choose which treatment the patient receives. This avoids bias towards one treatment and also ensures there is an equal mix of patients of different ages, sex and states of health in each group.

Clinical trials typically include trials at three different phases, generally referred to as Phase I, II or III. Each phase answers different questions about the new treatment. The Myeloma XI trial is a Phase III trial which is designed specifically to compare new treatment combinations with the current standard treatment combination in a large group of patients.

For more information see the Clinical Studies Infoguide from Myeloma UK. To order a free copy call the Myeloma Infoline on 0800 980 3332. This information is also available to download at www.myeloma.org.uk
Previous national myeloma trials in the UK

The first large-scale myeloma clinical trials in the UK were initiated in the early 1960s by the UK Medical Research Council (MRC) following the introduction of the chemotherapy drug melphalan. Today, the MRC and other medical charities work in partnership with the National Cancer Research Institute (NCRI) and the National Cancer Research Network (NCRN) to improve cancer research and cancer treatment throughout the UK.

These trials have been responsible for some notable discoveries and achievements that have improved the understanding and characterisation of myeloma and its treatment and management.

These achievements include:

- Specifying paraprotein levels in blood and urine
- Identifying the secondary effects of myeloma especially in relation to bone and the kidneys
- Recognising the crucial importance of a high fluid intake to help prevent kidney damage
- The introduction of high-dose therapy and autologous stem cell transplantation to the treatment options for myeloma
- The introduction of thalidomide as part of an initial combination treatment option for patients
- Discovering that inclusion of the bisphosphonate zoledronic acid (previously known as Zometa®) to a standard initial treatment combination offers additional anti-myeloma effects and improves survival in newly diagnosed patients over and above its effects against myeloma bone disease

Table 1 on page 10 provides a brief overview of recent national myeloma trials and their outcomes.
<table>
<thead>
<tr>
<th>Trial</th>
<th>Start to time of analysis</th>
<th>Trial outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>MRC Myeloma V</td>
<td>June 1986 – Sept 1990</td>
<td>ABCM* treatment combination is superior to melphalan alone</td>
</tr>
<tr>
<td>MRC Myeloma V and VI linked bisphosphonate trial</td>
<td>June 1986 – May 1994</td>
<td>Long-term bisphosphonate treatment (sodium clodronate) slows progression of bone disease</td>
</tr>
<tr>
<td>MRC Myeloma VII for all patients under 65 years old</td>
<td>Oct 1993 – Oct 2000</td>
<td>High-dose therapy and stem cell transplantation is superior to conventional low-dose treatment</td>
</tr>
<tr>
<td>MRC Myeloma IX for patients of all ages</td>
<td>May 2003 – Nov 2007</td>
<td>Undergoing long-term follow up</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Data to date show that addition of thalidomide to standard treatment and the monthly infusion of the bisphosphonate, zolendronic acid, provide greater benefit. Thalidomide maintenance treatment is also beneficial to sub-groups of patients</td>
</tr>
<tr>
<td>NCRI Myeloma X for relapsed patients</td>
<td>Nov 2007 – ongoing</td>
<td>Trial ongoing</td>
</tr>
</tbody>
</table>

* ABCM – Adriamycin®, carmustine, cyclophosphamide, melphalan
What is the Myeloma XI trial trying to find out?

Before describing the Myeloma XI trial, it is important to gain an understanding of the previous Myeloma IX trial as the overall aims and design of the Myeloma XI trial are very similar to the Myeloma IX trial. The following provides a short summary of the Myeloma IX trial and the purpose of the Myeloma XI trial.

Background to the Myeloma IX trial:

The Myeloma IX trial, which completed patient recruitment in November 2007 and is now under long-term follow up, was designed for newly diagnosed patients of all ages.

The trial was comprised of two distinct treatment pathways: one for younger (under 70 years of age) and/or fitter patients involving high-dose therapy and stem cell transplantation and one for older (over 70 years of age) and/or less fit patients that did not involve high-dose therapy and stem cell transplantation.

The main aim of that trial was to determine if a thalidomide-containing initial treatment combination was more effective than standard initial treatment without thalidomide.

The results showed that thalidomide combinations were more effective than non-thalidomide combinations as initial treatment both for younger and/or fitter patients who went on to receive high-dose therapy and stem cell transplantation and for older and/or less fit patients who did not receive high-dose therapy and stem cell transplantation.

As a consequence of the trial, thalidomide combinations are now recommended for newly diagnosed patients and are considered to be the standard against which new drugs are compared.

In addition, the Myeloma IX trial was the first head-to-head trial to be carried out which showed that monthly infusion of the bisphosphonate drug zoledronic acid was much more effective in preventing bone loss and fractures than the daily ingestion of Bonefos® (sodium clodronate).
Furthermore, zolendronic acid also increased the length of remission in patients, demonstrating for the first time that it offered additional anti-myeloma benefits over and above the known effects against myeloma bone disease.

More recently, newer drugs such as Velcade® (bortezomib) and Revlimid® (lenalidomide) have been approved for use in myeloma. Velcade is the first of a new type of cancer drug called proteasome inhibitors. Revlimid is a thalidomide derivative and is classed as an immunomodulatory drug (IMiD).

Both drugs have been shown to be very effective in treating myeloma patients who have relapsed after several previous treatments. However, there is still a need to better understand their effectiveness and efficacy in newly diagnosed patients.

Velcade and Revlimid are now approved for routine use as second-line or third-line treatment respectively for patients in England and Wales whose myeloma has returned. Velcade is also approved for use as a first-line treatment in combination with a chemotherapy drug and a steroid for patients who are unable to undergo high-dose therapy and stem cell transplantation or who are unable to take thalidomide for various reasons.

In Scotland, Velcade is approved as a first-line treatment option in combination with melphalan and prednisolone and also for use in all subsequent stages of treatment.

Revlimid does not yet have approval for use as initial treatment for newly diagnosed myeloma patients as research is still ongoing to understand the best ways of using it in this setting.

Vorinostat is a new type of drug known as a histone deacetylase (HDAC) inhibitor which is currently being investigated as a new treatment for myeloma. Evidence suggests that vorinostat works best when it is combined with other anti-myeloma treatments but so far it has been tested mostly in relapsed myeloma patients.
Purpose of the Myeloma XI trial

The purpose of the Myeloma XI trial is to compare thalidomide, Revlimid, and Velcade combinations in newly diagnosed patients of all ages. The aim is to determine whether Revlimid or thalidomide-containing treatment is best and then to identify which sequence of treatment combinations that potentially offers improved benefit to myeloma patients is best.

The trial intends to answer key questions at three different stages of treatment:

- Is a Revlimid-containing initial treatment more effective and does it have fewer side-effects than a thalidomide-containing one?
- Does Velcade-containing consolidation treatment help those who have not responded well to the initial treatment?
- Does maintenance treatment with Revlimid alone, or in combination with vorinostat, increase the time the myeloma remains stable after initial treatment, and prolong survival?

The trial is looking at the effects of these treatments on myeloma in terms of response to treatment, the extent to which the treatments can prevent the progression of myeloma and the extent to which the treatments can prolong overall survival.

To include patients of all ages, researchers have divided the Myeloma XI trial into two categories in the same way as the Myeloma IX trial:

- An intensive pathway for younger and/or fitter patients which includes high-dose therapy and autologous stem cell transplantation
- A non-intensive pathway for older and/or less fit patients which does not include high-dose therapy and autologous stem cell transplantation

More information about the difference between the two treatment pathways can be found on page 23. Each of the pathways is explained in detail on pages 36 – 37.
Version 6 protocol
The latest version of the trial also aims to find out whether younger/fitter patients will do better with a four-drug combination for initial treatment. The four-drug combination includes a new drug called Kyprolis® (carfilzomib). This is to find out whether the use of an additional drug will prevent, or delay, relapse.

Patients on the four-drug combination will not receive consolidation treatment. If they have not responded to treatment they will be withdrawn from the trial. All other patients will be randomised to receive Velcade-containing consolidation or no consolidation.

The new version of the trial does not include vorinostat as an option during maintenance. Patients will receive Revlimid maintenance or no maintenance.
Which myeloma patients are eligible to take part?

The Myeloma XI trial is for newly diagnosed patients with symptomatic myeloma and requiring treatment as a result.

Symptomatic myeloma means that the myeloma is causing complications such as myeloma bone disease, anaemia and kidney damage.

To take part in this trial, patients must also meet other eligibility criteria:

- Patients who have not had any treatment for myeloma, other than localised radiotherapy, bisphosphonates or short-term steroids
- Patients who have no significant pre-existing liver, kidney, lung, marrow and heart damage
Things to consider before deciding whether to take part in the trial

Before deciding whether to take part in the Myeloma XI trial, it is important that patients understand what is involved so they can make an informed decision about whether or not to take part.

This includes knowing and understanding the trial treatments and tests involved; the potential advantages and disadvantages of each stage of treatment; how long the trial will take and why it is being done.

Understanding what is involved may include:

- Reading information specifically related to the trial, provided by the doctor or nurse involved in the trial, describing what is involved and what one should expect
- Reading information about the trial and the treatments involved from other reliable sources such as Myeloma UK
- Talking to the doctor, research nurse, the Myeloma Infoline team at Myeloma UK and other patients
- Discussing the trial and/or treatment with family and friends

It may help to understand what other treatment options are available should patients decide not to take part and the potential risks and benefits of each.

Entering into the trial should not be taken lightly and all patients will be given the opportunity and time to discuss every aspect of the trial in detail before making a decision. Each patient is different and will have their own priorities, concerns and lifestyle – all of which can play a significant part in making their decision.

Taking part in the trial is entirely voluntary. Patients do not have to take part and do not have to give a reason. Treatment and care is unlikely to be affected in any way if patients decide not to take part. They will still be entitled to the currently available treatment for myeloma that is most suitable for them.
Even when patients decide to take part, in most cases, they are free to withdraw from the trial at any time although some follow-up may be needed on the original trial treatment. Depending on the stage of the trial, withdrawal may not be possible immediately if treatment is still on-going or if stopping straight away may be considered harmful.
What are the potential advantages and disadvantages of being in the trial and of the trials treatments?

The aim of the Myeloma XI trial is to determine the most effective treatments for newly diagnosed myeloma patients, how best they can be used and how they compare with each other. However, it cannot be assumed that a new treatment or a new combination of current treatments is better than the current standard treatment, so research trials need to be done to find this out. In doing so, important questions can be answered which may help improve treatment for future patients.

The following describes some of the potential advantages and disadvantages of taking part in this trial.

Potential advantages:

Patients taking part are more closely monitored during and after the trial, have regular tests and may be asked some extra questions about how they are feeling. This means that any changes – whether or not they are directly related to the trial treatment they are taking or to other factors – will be noticed and treated promptly.

In taking part, patients have a 50% chance of receiving Revlimid as part of their initial treatment, which they would not be able to get outside of this trial. They may also be able to receive Velcade consolidation treatment if they do not respond well to initial treatment and then a 33% chance of having maintenance treatment with Revlimid or a 33% chance of having Revlimid in combination with vorinostat.

Neither consolidation nor maintenance treatment is approved for myeloma patients outside of a clinical trial setting. Likewise, vorinostat is not yet licensed as an anti-myeloma treatment and being on the Myeloma XI trial offers the opportunity, if randomised, to receive it as part of maintenance treatment.

The Myeloma XI trial is being overseen by an expert committee whose role is to continually review the trial data being collected and to assess whether there are any safety issues that should be brought to the attention of the doctor or nurse. If it becomes apparent that one of the treatment approaches or combinations is much better or worse than the other, the expert committee may consider stopping the trial early. In such cases all patients will, if suitable, have their treatment changed to the better treatment.
Potential disadvantages:

The Myeloma XI trial involves different treatment pathways in which patients are randomised to particular treatment pathways (see page 22 for an explanation). Some patients may consider being randomised to the standard treatment pathway a potential disadvantage. However, it is worth bearing in mind that there is no guarantee the new treatments in the trial will work better than the standard treatments they are being compared to.

On a practical level, if patients are taking part in the intensive pathway, it is possible that they may have to travel to another hospital to prepare for and have their high-dose therapy and stem cell transplant. This may be a significant issue for some patients and their families. It is important therefore for patients to talk this through with their doctor so they know exactly what will be required in terms of travel.

As with most treatments for myeloma, the treatments in this trial have the potential to cause side-effects. These are explained to patients by their doctor or nurse. It is important that the potential side-effects of treatment are acceptable to patients and do not affect their quality of life to the extent that the side-effects outweigh the benefits of treatment, either in the short term or long term.

Version 6 protocol

Patients being treated on the intensive pathway may receive a four-drug initial treatment combination including Kyprolis, which they would not be able to get outside of this trial.

Patients on the four-drug initial treatment combination will not be given consolidation.

All patients in the new trial will be randomised to either receive Revlimid maintenance or no maintenance. Unlike the previous protocol, no patients will receive maintenance which includes vorinostat maintenance.
What happens next when patients decide to take part?

If patients decide to take part in the trial a number of things need to be done before treatment can be started.

Patients are asked to sign an Informed Consent Form. This is a form which explains the potential risks and benefits of taking part in the trial. Informed consent is explained in more detail in the next section.

To determine whether patients can take part in the trial, they may need to undergo some pre-trial medical tests. These may include:

- Blood tests
- Urine tests
- **Bone marrow** biopsy
- X-rays or other scans
- Pregnancy test (if patient is of childbearing potential)

Results from these tests will provide baseline information to assess each patient’s myeloma and general health prior to starting treatment. These tests will be repeated regularly and the information used to measure patients’ response to treatment.

If patients decide to take part, any trial-related information about them is kept strictly confidential and they will not be identified in any report or publication about the trial.
What is informed consent?

Informed consent is formal confirmation that patients understand what is involved in the trial and that they give permission for the hospital staff to administer the trial treatment.

For consent to be valid it needs to be given freely, with patients having had enough information to enable them to make a decision. Patients who have specific requirements, e.g. patients with sight difficulties or patients whose first language is not English, should be able to obtain the same information in an appropriate format.

If patients consent, they are asked to sign an Informed Consent Form.

Before deciding to take part, patients need to understand what the trial is trying to find out and how they will be treated. It is important that they ask questions and they are given enough time to consider all the potential implications, both now and in the future, of being involved in the trial.

Examples of relevant questions patients may want to ask their doctor or nurse can be found in the Questions for the doctor or nurse section on page 55.
Do patients have a say in what treatment they receive?

Each patient’s doctor or nurse will discuss with them which treatment pathway, the intensive or non-intensive, is most suitable for them. Once this has been agreed, randomisation is used to decide which treatments they receive from within that pathway. This means that neither patients nor their doctor can choose which treatments patients receive.

All the treatments used in the Myeloma XI trial have been individually shown to be effective in treating myeloma and their safety profile is well understood.

Randomisation is used to decide:

- Which initial treatment patients will have
- Whether patients receive consolidation treatment or not if they have only responded partially to initial treatment
- Whether or not patients receive maintenance treatment either with Revlimid alone or Revlimid plus vorinostat

It is important for patients to understand that they are free to decide to withdraw from the trial at any time. Withdrawing from the trial is discussed in more detail on page 51.

Version 6 protocol
Patients on the four-drug combination will not receive consolidation. Other patients may receive consolidation depending on the results of their initial treatment and randomisation.

All patients in the new trial will be randomised to receive either Revlimid maintenance or no maintenance. No patients will receive vorinostat maintenance.
What is the difference between the two treatment pathways?

As described earlier, the Myeloma XI trial is divided into two treatment pathways: intensive and non-intensive. The main difference between them is that the intensive pathway includes high-dose therapy and stem cell transplantation.

High-dose therapy and stem cell transplantation is usually only an option for younger and/or fitter patients, generally up to the age of 70.

For older and/or less fit patients, decisions about high-dose therapy and stem cell transplantation are based on a range of factors including their general state of health. High-dose therapy and stem cell transplantation is normally not recommended for patients over 70 years of age, as the possible advantages are often outweighed by the potential disadvantages.

If high-dose therapy and stem cell transplantation is not considered to be suitable for patients, or if patients decide against it, then they are offered the non-intensive treatment pathway which does not involve high-dose therapy and stem cell transplantation.

Another difference is in the dose of the initial treatment. In both pathways a standard myeloma treatment combination is being compared to a new treatment combination. However, one or more of the treatments is given at a lower (attenuated) dose in the non-intensive pathway as patients in this group may not be able to tolerate a higher dose of treatment.

There are also similarities between the treatment pathways. In both pathways, patients who do not respond well to the initial treatment combination after four to six cycles may go on to receive a Velcade-containing consolidation treatment and either maintenance or no maintenance treatment.

Details about the treatment on each of the two pathways are given in the following sections.
Version 6 protocol
Patients being treated on the intensive pathway may receive a four-drug initial treatment combination including Kyprolis, which they would not be able to get outside of this trial. Patients who receive the four-drug combination will not receive consolidation.

Patients being treated on the new protocol will either have Revlimid maintenance or no maintenance. They will not have vorinostat maintenance.
Treatments used in the intensive pathway

The intensive pathway is divided into four main stages – each stage is described in more detail in this section. The design of the intensive pathway is summarised at the end of this section in Figure 1.

Stage 1: Induction treatment

Initial treatment given prior to high-dose therapy and stem cell transplantation is referred to as induction treatment. On the intensive pathway, patients receive one of two induction treatment combinations, either a current standard treatment combination:

- CTD – cyclophosphamide, thalidomide and dexamethasone

or a new treatment combination:

- CRD – cyclophosphamide, Revlimid and dexamethasone

CTD is the current standard induction treatment combination given to newly diagnosed myeloma patients. In clinical trials, CRD has previously been shown to be effective in patients whose myeloma has relapsed and who need further treatment. However, the effect of CRD in newly diagnosed myeloma is less well established. Consequently there is a need to find out more about how CRD compares to the current standard induction treatment, CTD.

CTD (Table 2), CRD (Table 3) combinations are given in treatment cycles:

- The CTD treatment cycle lasts 21 days without a break in treatment before the next cycle starts

- The CRD treatment cycle lasts 28 days, made up of three weeks of treatment and a one week break in treatment before the next cycle starts

Treatment continues until a maximum response is achieved and patients receive between four and six cycles of treatment unless their myeloma is progressing or they are unable to tolerate the treatment.
Table 2 – The CTD treatment combination

<table>
<thead>
<tr>
<th>CTD combination (21 day treatment cycle)</th>
<th>Name of drug</th>
<th>Type of drug</th>
<th>How it is given</th>
<th>How often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Chemotherapy</td>
<td>By mouth</td>
<td>Once a week (days 1, 8 &amp; 15 of each cycle)</td>
<td></td>
</tr>
<tr>
<td>Thalidomide</td>
<td>IMiD</td>
<td>By mouth</td>
<td>Daily throughout the cycle</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Steroid</td>
<td>By mouth</td>
<td>Days 1 – 4 and 12 – 15 of each cycle</td>
<td></td>
</tr>
</tbody>
</table>

Table 3 – The CRD treatment combination

<table>
<thead>
<tr>
<th>CRD combination (28 day treatment cycle)</th>
<th>Name of drug</th>
<th>Type of drug</th>
<th>How it is given</th>
<th>How often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Chemotherapy</td>
<td>By mouth</td>
<td>Days 1 and 8 of each cycle</td>
<td></td>
</tr>
<tr>
<td>Revlimid</td>
<td>IMiD</td>
<td>By mouth</td>
<td>Daily for the first 21 days of each cycle</td>
<td></td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Steroid</td>
<td>By mouth</td>
<td>Days 1 – 4 and 12 – 15 of each cycle</td>
<td></td>
</tr>
</tbody>
</table>
Version 6 protocol

Patients being treated on the intensive pathway may receive a four-drug initial treatment combination:

- CCRD – Kyprolis, cyclophosphamide, Revlimid and dexamethasone

Kyprolis is a new type of proteasome inhibitor drug, similar to Velcade. The four drugs in CCRD all work in different ways and the trial aims to find out whether this offers better results than CTD or CRD, with acceptable side-effects.

CCRD treatment cycles:

- The CCRD treatment cycle lasts 28 days, made up of three weeks of treatment and a one week break in treatment before the next cycle starts

<table>
<thead>
<tr>
<th>Name of drug</th>
<th>Type of drug</th>
<th>How it is given</th>
<th>How often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kyprolis</td>
<td>Proteasome inhibitor</td>
<td>Intravenously</td>
<td>Days 1 and 2, 8 and 9, and 15 and 16 (only on days 1 and 2 in first cycle)</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Chemotherapy</td>
<td>By mouth</td>
<td>Days 1 and 8 of each cycle</td>
</tr>
<tr>
<td>Revlimid</td>
<td>IMiD</td>
<td>By mouth</td>
<td>Daily for the first 21 days of each cycle</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Steroid</td>
<td>By mouth</td>
<td>Days 1 – 4, 8, 9 and 15, 16 of each cycle</td>
</tr>
</tbody>
</table>
Cyclophosphamide, thalidomide, Revlimid and dexamethasone all have different but synergistic and complementary mechanisms of action. This means that they work in different ways but when combined with the other treatments, they become more effective at killing the myeloma cells. The way each treatment is thought to work is described below:

- **Cyclophosphamide** – is a chemotherapy drug and works by interfering with the way cells grow and divide. This results in cell death. Cyclophosphamide particularly targets rapidly dividing cells such as myeloma cells causing myeloma cell death.

- **Thalidomide** – has several mechanisms of action that affect myeloma cells. It can stop the growth and survival of myeloma cells in several different ways and can prevent the growth of new blood vessels. It is also known to alter the way the immune system works by boosting the immune response against myeloma cells.

- **Revlimid** – like thalidomide has several mechanisms of action that affect myeloma cells in a similar way.

- **Dexamethasone** – is a synthetic steroid which has multiple actions in the body as it mimics naturally occurring hormones called glucocorticoids. Dexamethasone is used to treat myeloma because of its ability to cause myeloma cell death.

**Version 6 protocol**

Kyprolis – works by blocking (inhibiting) the proteasomes, which are large molecules that are present in all cells in the body. They are involved in the removal, breakdown and recycling of damaged proteins or those that are no longer needed by the cell. Myeloma cells are particularly sensitive to this type of drug.

For more information about the treatments see the *Cyclophosphamide, thalidomide and dexamethasone (CTD)* and *Revlimid* Infoguides, and the *Kyprolis (carfilzomib)* Horizons Infosheet from Myeloma UK. To order a free copy, contact the *Myeloma Infoline* on 0800 980 3332. This information is also available to download at [www.myeloma.org.uk](http://www.myeloma.org.uk).
Prescribing, storing and taking thalidomide and/or Revlimid

All patients need to sign a registration form and an additional Informed Consent Form relating to thalidomide and Revlimid treatment. Thalidomide has in the past caused birth defects (phocomelia) and as Revlimid is structurally similar, the use of both drugs is therefore very carefully controlled.

Both thalidomide and Revlimid are regulated by their manufacturer under separate risk management programmes designed to prevent exposing unborn babies to thalidomide and/or Revlimid. These programmes are mandatory requirements before either thalidomide or Revlimid can be considered for approval by the regulatory authorities. Both programmes are the responsibility of Celgene Corporation, the company that markets both drugs. The two programmes have similar components but also key differences regarding the distribution and dispensing of thalidomide and Revlimid.

All patients must enrol and comply with the relevant programme when receiving thalidomide or Revlimid. These programmes are fully explained to patients before treatment is started. Patients are also required to answer a set of questions but these may differ from patient to patient depending on their individual circumstances.

As part of the programme, female patients of childbearing potential are required to have regular pregnancy tests. As thalidomide and Revlimid can be present in semen, male patients are asked to use a condom when engaging in sexual activity with a female partner of childbearing potential.

Patients, particularly if they are older, may question whether parts of these risk management programmes should apply to them. These programmes are in place to control all prescriptions of thalidomide and Revlimid, to ensure that patients are aware of the potential dangers of these drugs and that they are prescribed, handled, used and stored safely. Therefore, all patients, regardless of age, must register and comply with these programmes.
Stage 2: Consolidation treatment

The aim of consolidation treatment is to induce a deeper, longer remission by suppressing the level of the myeloma further.

If patients respond well to CTD or CRD, they do not receive consolidation treatment but go on to receive high-dose therapy and a stem cell transplant (see Stage 3 below).

If patients do not respond or if their myeloma continues to progress following CTD or CRD, then they will automatically be given consolidation treatment consisting of a combination of Velcade, cyclophosphamide and dexamethasone (VCD).

If patients subsequently respond well to the VCD treatment combination they will proceed to high-dose therapy and stem cell transplantation. However, if patients do not respond well to VCD, then they are required to leave the trial and their doctor will discuss other treatment options available outside of the trial.

For patients who respond partially to CTD or CRD but who do not achieve the desired response, they will be randomised to receive either VCD or no treatment. It is currently unclear if there is any benefit in giving additional treatment to this group of patients, so the aim of this part of the trial is to determine whether there is or not.

Each VCD treatment cycle lasts 21 days (Table 4) and patients have up to eight cycles depending on how well they respond and any side-effects they get. If patients are randomised to not having additional treatment then they go on to receive high-dose therapy and stem cell transplantation.
Stage 3: High-dose therapy and stem cell transplantation

A good response to induction and/or consolidation treatment means that patients can go on to receive high-dose therapy and autologous stem cell transplantation.

High-dose therapy consists of treatment with the chemotherapy drug, melphalan, the aim of which is to further reduce the number of remaining myeloma cells. However, the dose of melphalan used is such that normal bone marrow cells are killed as well as the myeloma cells. Therefore, patients need to have a stem cell transplant, using their own stem cells, afterwards to restore bone marrow function and enable it to make new blood cells again.

High-dose therapy and stem cell transplantation is a relatively intensive procedure. Although it is safe and may potentially help to improve the duration, depth and quality of response when used in conjunction with anti-myeloma treatment, it is associated with potentially more side-effects and a longer recovery period than anti-myeloma treatment alone.

The following looks at the different stages of the stem cell transplant process.
1. Stem cell mobilisation

After completing induction or consolidation treatment, patients prepare for stem cell collection by first ensuring they have an adequate amount of stem cells in their blood.

Normally the levels of stem cells present in the blood are low and to collect enough for transplant, it is necessary to have treatment to increase the number of stem cells produced and released from the bone marrow into the blood.

This process, known as stem cell mobilisation, involves treatment with cyclophosphamide, but at a higher dose than when given with CTD or CRD. This is given together with daily injections of a growth factor called granulocyte-colony stimulating factor (G-CSF) for approximately a week. Together, high-dose cyclophosphamide and G-CSF treatment increases the production of stem cells in the bone marrow, causing them to ‘spill over’ into the blood, where they can be collected more easily.

To make sure there are enough stem cells in the blood for collection to take place, a CD34+ blood test is performed towards the end of the course of G-CSF treatment. CD34+ is the technical name given to a surface protein found on stem cells and provides a useful way of tagging them. This enables the number of stem cells in the blood to be counted.

Although stem cell mobilisation with cyclophosphamide and G-CSF is generally successful in the majority of patients, a small proportion of patients unfortunately fail to mobilise enough stem cells for collection. In such cases, Mozobil® (plerixafor) may be used in combination with G-CSF to try to enhance stem cell mobilisation. Mozobil is a new type of drug which aids the release of stem cells into the blood.

If stem cell mobilisation is still not successful, patients may still go on to receive melphalan chemotherapy (see below) but at a lower dose and without a stem cell transplant. Alternatively, their doctor may recommend using a treatment outside of the trial. In either case, patients will be asked to continue attending the outpatient clinic for monitoring.
2. Stem cell collection

Collecting stem cells from the blood is done as an outpatient at a specialist transplant centre within a hospital by a process called apheresis. This involves blood being removed from a vein in the patient's arm and passed through a machine that separates and collects stem cells. The remainder of the blood is returned to the patient through a vein in the other arm.

Sometimes enough stem cells are collected in one session but more commonly two or three sessions over consecutive days may be needed. Each session lasts approximately three to four hours. The minimum number of stem cells needed for a successful transplant is two million stem cells per kilogram of body weight.

Once enough stem cells have been collected, they are frozen and stored.

3. High-dose chemotherapy with melphalan

The next step involves patients receiving high doses of the chemotherapy drug, melphalan, over the course of a single day. Fluids and various drugs are also given before, during and after the high-dose melphalan treatment, to help reduce potential side-effects.

4. Stem cell transplantation

The day after high-dose melphalan is administered, the previously collected stem cells are returned to the patient via a catheter into the blood stream. This is a relatively straightforward procedure which takes on average about one hour to complete and is similar to having a blood transfusion.

To help the transplanted stem cells graft in the bone marrow and start making new blood cells, patients may receive further injections of G-CSF to help with the engraftment process.
High-dose therapy and stem cell transplantation takes place only at specialist transplant centres and patients are expected to be in hospital for 3 – 4 weeks. During this time they may feel quite unwell and are kept in protective isolation and given antibiotics to avoid infection. Most patients remain in hospital until their blood counts return to normal. Once at home, recovery time may last between 3 – 6 months.

For more information on autologous stem cell transplants, see the Myeloma UK High-Dose Therapy and Autologous Stem Cell Transplantation Infoguide. To order a free copy, contact the Myeloma Infoline on 0800 980 3332. This information is also available to download at www.myeloma.org.uk

Stage 4: Maintenance treatment

After a minimum period of six weeks following the transplant procedure, patients are randomised again to one of three groups:

- No maintenance treatment (as per current standard UK practice) or
- Revlimid only as a maintenance treatment, given orally for 21 days of a 28 day cycle, until the myeloma returns or
- Revlimid in combination with vorinostat as a maintenance treatment until the myeloma returns. Revlimid is given orally for 21 days of a 28 day cycle and vorinostat is given orally every day for a week, every other week during the 28 day cycle

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Patients being treated on the new protocol will either have Revlimid maintenance or no maintenance. They will not have vorinostat maintenance.
If allocated to receive maintenance treatment, patients begin this approximately three months after transplantation.

All patients are monitored regularly regardless of whether they are on maintenance treatment or not, but those who are on maintenance treatment may require more frequent monitoring and more hospital visits.

If patients are randomised to receive maintenance treatment, they are asked to sign an additional Informed Consent Form and a Revlimid registration form as part of the risk management programme as described on pages 29 – 30, if they have not had Revlimid already.
Figure 1 – An overview of the intensive pathway

Stage 1
- Cyclophosphamide
- Thalidomide
- Dexamethasone
- Revlimid
- Dexamethasone

Stage 2
- If the myeloma has not responded well or has got worse:
  - Velcade
  - Cyclophosphamide
  - Dexamethasone
- If the myeloma has responded very well:
  - Revlimid
  - Dexamethasone
- If the myeloma has responded partially:
  - Randomisation to consolidation treatment
    - Velcade
    - Cyclophosphamide
    - Dexamethasone
    - No consolidation treatment

Stage 3
- High-dose therapy and stem cell transplantation

Stage 4
- Randomisation to maintenance treatment
  - No maintenance
  - Revlimid maintenance
  - Revlimid plus vorinostat maintenance
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Figure 1 – An overview of the intensive pathway

Stage 1
- Randomisation to induction treatment
  - Cyclophosphamide
  - Thalidomide
  - Dexamethasone
  - Revlimid
  - Cyclophosphamide
  - Dexamethasone
  - Kyprolis
  - Cyclophosphamide
  - Revlimid
  - Dexamethasone

Stage 2
- If the myeloma has not responded well or has got worse
  - Velcade
  - Cyclophosphamide
  - Dexamethasone
- If the myeloma has responded very well
  - Randomisation to consolidation treatment
    - Velcade
    - Cyclophosphamide
    - Dexamethasone
    - No consolidation treatment

Stage 3
- High-dose therapy and stem cell transplantation

Stage 4
- Randomisation to maintenance treatment
  - No maintenance
  - Revlimid maintenance
Treatments used in the non-intensive pathway

The non-intensive pathway is divided into three main stages – each stage is described in more detail below. The design of the non-intensive pathway is summarised at the end of this section in Figure 2.

Stage 1: Initial treatment

Patients are randomised to receive one of two initial treatment combinations, either a current standard treatment combination:

- CTD – cyclophosphamide, thalidomide and dexamethasone or a new treatment combination:
- CRD – cyclophosphamide, Revlimid and dexamethasone

CTDa is the current standard treatment combination given to newly diagnosed myeloma patients who are not eligible for high-dose therapy and stem cell transplantation. CRDa has been shown to be effective in patients whose myeloma has returned and who need further treatment. However, the effect of CRDa in newly diagnosed myeloma is less well established. There is, therefore, a need to find out more about how CRDa compares to the established treatment combination CTDa.

The ‘a’ stands for attenuated, which means that the dose of dexamethasone used in the non-intensive pathway is lower than that used in the intensive pathway.

The starting dose of thalidomide may also be lower and gradually increased to the same dose used in the intensive pathway. This is so that patients in the non-intensive pathway, who are older and/or less fit, can tolerate the treatment better. There is no attenuation of the dose of Revlimid as it is generally well tolerated even in older and/or less fit patients.

Both the CTDa and CRDa treatment combinations are given in treatment cycles. Both treatment cycles last 28 days. Patients receive a minimum of six cycles, depending on their response to treatment.
For more information about how each of the treatments work, see page 28.
The CTDa and CRDa treatment combinations are summarised in Tables 5 and 6 below.

**Table 5 – The CTDa treatment combination**

<table>
<thead>
<tr>
<th>Name of drug</th>
<th>Type of drug</th>
<th>How it is given</th>
<th>How often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Chemotherapy</td>
<td>By mouth</td>
<td>Days 1, 8, 15 and 22 of each cycle</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>IMiD</td>
<td>By mouth</td>
<td>Daily throughout the cycle</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Steroid</td>
<td>By mouth</td>
<td>Days 1 – 4 and 15 – 18 of each cycle</td>
</tr>
</tbody>
</table>

**Table 6 – The CRDa treatment combination**

<table>
<thead>
<tr>
<th>Name of drug</th>
<th>Type of drug</th>
<th>How it is given</th>
<th>How often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Chemotherapy</td>
<td>By mouth</td>
<td>Days 1 and 8 of each cycle</td>
</tr>
<tr>
<td>Revlimid</td>
<td>IMiD</td>
<td>By mouth</td>
<td>Daily for the first 21 days of each cycle</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Steroid</td>
<td>By mouth</td>
<td>Days 1 – 4 and 15 – 18 of each cycle</td>
</tr>
</tbody>
</table>
Prescribing and taking thalidomide and/or Revlimid

All patients need to sign a registration form and an additional Informed Consent Form relating to thalidomide and Revlimid treatment. Thalidomide has in the past caused birth defects (phocomelia) and as Revlimid is structurally similar, the use of both drugs is therefore very carefully controlled.

Both thalidomide and Revlimid are regulated by their manufacturer under separate risk management programmes designed to prevent exposing unborn babies to thalidomide and/or Revlimid. These programmes were mandatory requirements before either thalidomide or Revlimid could be considered for approval by the regulatory authorities. Both programmes are the responsibility of Celgene Corporation, the company that markets both drugs. The two programmes have similar components but also key differences regarding the distribution and dispensing of thalidomide and Revlimid.

All patients must enrol and comply with the relevant programme when receiving thalidomide or Revlimid. These programmes are fully explained to patients before treatment is started. Patients are also required to answer a set of questions but these may differ from patient to patient depending on their individual circumstance.

As part of the programme, female patients of childbearing potential are required to have regular pregnancy tests. As thalidomide and Revlimid can be present in semen, male patients are asked to use a condom when engaging in sexual activity with a female partner of childbearing potential.

Patients, particularly if they are older, may question whether parts of these risk management programmes should apply to them. These programmes are in place to control all prescriptions of thalidomide and Revlimid, to ensure that patients are aware of the potential dangers of these drugs and that they are prescribed, handled, used and stored safely. Therefore, all patients, regardless of age must register and comply with these programmes.
Stage 2: Consolidation treatment

The aim of consolidation treatment is to reduce the level of myeloma further.

If patients respond well to CTDa or CRDa, they do not receive consolidation treatment but go on to be randomised to receive maintenance treatment (as described in the next section) or no further treatment.

If patients do not respond to CTDa or CRDa, or if their myeloma continues to progress following CTDa or CRDa, they are automatically given consolidation treatment consisting of a combination of Velcade, cyclophosphamide and dexamethasone (VCD).

If patients respond well to the VCD treatment combination they are then randomised to receive maintenance treatment or no treatment. However, if patients do not respond well to VCD, they are required to leave the trial and their doctor will discuss other treatment options outside of the trial with them.

For patients who respond partially to CTDa or CRDa but who do not achieve the desired response, they are then randomised to receive either VCD or no treatment. This is so that doctors can determine if there is any benefit in giving additional treatment to this group of patients as currently this is unclear.

Each VCD treatment cycle lasts 21 days (Table 7) and patients receive up to a maximum of eight cycles depending on how well they respond and any side-effects they get.

If patients are randomised to no consolidation treatment in the non-intensive pathway, they proceed to the maintenance randomisation stage.
Table 7 – The VCD treatment combination

<table>
<thead>
<tr>
<th>Name of drug</th>
<th>Type of drug</th>
<th>How it is given</th>
<th>How often</th>
</tr>
</thead>
<tbody>
<tr>
<td>Velcade</td>
<td>Proteasome inhibitor</td>
<td>By injection into a vein or into the skin</td>
<td>Days 1, 4, 8 and 11 of each cycle</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Chemotherapy</td>
<td>By mouth</td>
<td>Days 1, 8 and 15 of each cycle</td>
</tr>
<tr>
<td>Dexamethasone</td>
<td>Steroid</td>
<td>By mouth</td>
<td>Days 1 – 2, 4 – 5, 8 – 9 and 11 – 12 of each cycle</td>
</tr>
</tbody>
</table>

Stage 3: Maintenance treatment

Patients who have achieved a maximum response to initial and consolidation treatment and who are eligible, are randomised to one of three groups:

- No maintenance treatment (as per current standard UK practice) or
- Revlimid only as a maintenance treatment, given orally for 21 days of a 28 day cycle, until the myeloma returns or
- Revlimid in combination with vorinostat as a maintenance treatment until the myeloma returns. Revlimid is given orally for 21 days of a 28 day cycle and vorinostat is given orally every day for a week, every other week during the 28 day cycle

All patients receive follow-up care and monitoring. Those on maintenance treatment may require more frequent monitoring and more hospital visits.

If patients are randomised to receive maintenance treatment, they are asked to sign an additional Informed Consent Form and a Revlimid registration form as part of the risk management programme as described on pages 21 and 27, if they haven’t had Revlimid already.
Figure 2 – An overview of the non-intensive pathway

Stage 1
- Randomisation to initial treatment
  - Cyclophosphamide
  - Thalidomide
  - Revlimid
  - Dexamethasone
  - Velcade

Stage 2
- If the myeloma has not responded well or has got worse
  - Velcade
  - Cyclophosphamide
  - Dexamethasone
- If the myeloma has responded very well
  - Randomisation to consolidation treatment
    - Velcade
    - Cyclophosphamide
    - Dexamethasone
- If the myeloma has responded partially
  - No consolidation treatment

Stage 3
- Randomisation to maintenance treatment
  - No maintenance
  - Revlimid maintenance
  - Revlimid plus vorinostat maintenance
Patients being treated on the new protocol will either have Revlimid maintenance or no maintenance. They will not have vorinostat maintenance.

Figure 2 – An overview of the non-intensive pathway

Version 6 protocol
What are the potential side-effects of the trial treatments?

Some patients may have side-effects from the treatments they receive whilst on the Myeloma XI trial. All the treatments used have been studied independently and their common potential side-effects are known. These potential side-effects are explained to patients before treatment is started. Some of the more common side-effects of the treatments used are listed in Table 8 on page 46.

The vast majority of side-effects can be prevented. Those that do occur are usually mild and transient and can be treated and/or managed. If side-effects persist, treatment can be adjusted and the doses of the drugs patients receive can be reduced. In rare cases, if certain side-effects continue to persist after adjustments have been made, patients may be withdrawn from the trial.

Each patient’s progress is monitored carefully. Every time they go to hospital for treatment, they are asked about and assessed for any side-effects they have after or since the previous cycle of treatment.

Side-effects vary considerably from patient to patient. If patients have any side-effects it is important that they tell their doctor or nurse as soon as possible so they can be managed and/or treated.
Table 8 – Common side-effects of Myeloma XI treatments

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Potential side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyclophosphamide</td>
<td>Nausea, vomiting, hair thinning, mouth ulcers, diarrhoea, loss of appetite, infection, anaemia, bruising or bleeding, skin reactions, infertility</td>
</tr>
<tr>
<td>High-dose therapy (melphalan)</td>
<td>Nausea, vomiting, hair loss, mouth ulcers, diarrhoea, loss of appetite, infection, anaemia, bruising or bleeding, skin reactions, infertility</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>Birth defects if taken during pregnancy, drowsiness, blood clots, skin rash, constipation, tingling or numbness in fingers/toes (peripheral neuropathy)</td>
</tr>
<tr>
<td>Revlimid</td>
<td>Birth defects if taken during pregnancy, drowsiness, blood clots, diarrhoea, skin rash, fatigue, anaemia, decrease in blood counts, peripheral neuropathy (rare)</td>
</tr>
<tr>
<td>Steroids (dexamethasone)</td>
<td>Stomach irritation, increased appetite, swelling in hands and feet, increased blood sugar levels, infection, mood swings/irritability, difficulty in sleeping, muscle weakness</td>
</tr>
<tr>
<td>Velcade</td>
<td>Nausea, diarrhoea, vomiting, constipation, fatigue, decrease in blood counts, peripheral neuropathy, mild muscle pain, loss of appetite, difficulty in sleeping, dizziness</td>
</tr>
<tr>
<td>Vorinostat</td>
<td>Diarrhoea, constipation, nausea, vomiting, decrease in blood counts, fatigue, increased blood sugar levels, dizziness, headache, chills, fever, blood clots (rare)</td>
</tr>
<tr>
<td>G-CSF</td>
<td>Fever, aches and joint pain</td>
</tr>
<tr>
<td>Mozobil</td>
<td>Diarrhoea, nausea, dizziness, headache, joint pain, irritation/redness at injection site</td>
</tr>
</tbody>
</table>

**Version 6 protocol**
Possible side-effects of Kyprolis are bruising or bleeding, anaemia, infection or fatigue.
How long will the treatments in the Myeloma XI trial last?

The length of treatment depends on whether patients are on the intensive or non-intensive pathway and on the individual patient’s response to treatment. The length of the treatment including high-dose therapy and autologous stem cell transplantation for those on the intensive pathway is between 6 – 12 months. The length of the initial treatment for those on the non-intensive pathway depends on the response to treatment but is usually a minimum of 6 months. Those on consolidation treatment receive it for a maximum of 6 months.

If patients receive maintenance treatment, whether they are on the intensive or non-intensive treatment pathway, they take it until their myeloma shows signs of becoming active again (relapse). This will vary from patient to patient and could be a few months or several years.
Are additional tests/assessments done as part of the trial?

All patients are carefully monitored on a regular basis throughout the trial.

Most of the tests carried out as part of the monitoring process are the same as those for patients not taking part in the trial. However, there may be some additional tests that are specific to the trial. For example, some samples, such as blood and urine samples, will be collected and sent to central trial laboratories. The details of these additional tests are explained to patients before they enter the trial.

One of the aims of the Myeloma XI trial is to investigate the possible genetic factors responsible for the onset and progression of myeloma. The results of the genetic research will be used to develop better predictive and diagnostic tests so that more tailored treatments can be given and developed in the future to help improve patient outcomes.

This type of investigation requires DNA, RNA and protein to be studied. These are extracted from patients' blood and bone marrow samples already taken as part of their routine tests.

It is hoped this genetic information will identify features of myeloma that can be used to help predict a patient’s response to treatment or identify factors that may predispose a person to developing myeloma. Although patients taking part in the Myeloma XI trial may not personally benefit from these tests, the findings may be useful for future myeloma patients.

It is important to remember that these additional genetic tests are optional and even if patients choose to enter the main part of the trial, they may choose not to have these additional tests done. Patients who do wish to take part in these additional tests will be asked to sign an additional Informed Consent Form.

When the trial treatment has finished, patients continue to be carefully monitored by their doctor. They are asked to attend for regular check-ups every two months for the first two years, after which they will be asked to attend every three months.
What additional non-trial treatments need to be taken?

To deal with both symptoms and complications of myeloma and its treatments, patients may be given additional supportive treatments. However, these supportive treatments are not being assessed as part of the trial.

Each patient’s doctor will decide which additional treatments they need. For example, if patients are at an increased risk of developing blood clots in the form of a venous thrombotic event (VTE), deep vein thrombosis (DVT) or pulmonary embolism (PE), they may be prescribed treatment to prevent this whilst receiving their initial anti-myeloma treatment.

Most patients also receive a bisphosphonate drug. These are drugs used to slow down and prevent myeloma bone disease and form an important part of treatment for all myeloma patients.

Although there are a number of different types of bisphosphonate, zolendronic acid is the recommended treatment of choice in light of the recent Myeloma IX clinical trial, which showed that zolendronic acid was not only better than sodium clodronate (Bonefos) in treating myeloma bone disease, but also had anti-myeloma effects and improved survival.
What happens if the treatment in the trial doesn’t work?

The aim of treatment is to destroy as much of the myeloma as possible and help patients to feel as well as possible for as long as possible. Assessments are made each time patients visit the clinic to see how well the treatment has worked and to monitor the myeloma. Response to treatment is measured using blood tests although further bone marrow or X-ray tests may be required.

However, in rare cases it may be that patients do not respond well and their myeloma is not brought under control by the treatment they receive within the trial. This is likely to be a very disappointing and distressing time, both for patients and their families.

If at any point during the trial the doctor thinks the treatment is not working and another treatment is needed, they will discuss it with their patient. In some cases this may mean having to leave the trial, but in certain cases it may be possible to continue in the trial.
What if a patient wants to withdraw from the trial?

Patients are free to decide to withdraw from the Myeloma XI trial at any time. However, if they are already part way through treatment such as high-dose therapy and a stem cell transplant, it may not be possible to leave the trial immediately due to the potentially serious effects of stopping part way through treatment.

Notwithstanding this, there are two different ways of withdrawing from a trial:

- Patients may withdraw their consent to receive treatment as part of the trial. Any treatment patients are receiving as part of the trial is stopped at an appropriate point. They may continue to be monitored as part of the trial even though they will receive different treatment.

- Patients may withdraw their consent to receive treatment and for their data to be collected as part of the trial. Any treatment patients are receiving as part of the trial is stopped and data from their test results will only be recorded up to the point when their consent is withdrawn.

If patients are considering withdrawing from the trial, they should discuss the implications of doing so and all other treatment options that may be available to them fully with their doctor or nurse.

If patients decide to withdraw from the trial, their decision should not affect either their relationship with their doctor or future treatments they may receive or need.
The future

The results of the Myeloma XI trial will provide a greater understanding of the best way to treat newly diagnosed patients. More specifically, they will provide important information on:

- Whether Revlimid should be used in place of thalidomide as part of the initial treatment combination in newly diagnosed patients
- Whether Velcade should be given after initial treatment for patients who do not have a very good response to Revlimid or thalidomide, in an effort to improve the response and outcome for these patients
- Whether maintenance treatment with Revlimid can prolong the time myeloma is controlled after treatment or a stem cell transplant and improve the outcome for patients
- Whether including vorinostat in Revlimid maintenance treatment further improves the outcomes for patients
- What genetic factors contribute to the onset and progression of myeloma and how these might influence the choice of treatment for patients

As new ways of treating myeloma become available, different questions about the best way to treat it will need to be answered. Further national myeloma clinical trials will therefore follow.

The results of the Myeloma XI trial will be used to inform clinical practice and the development of clinical guidelines for the treatment of myeloma. Myeloma XI will be looking at long-term outcomes of treatment which means that the final report, normally published in a medical journal, may not be available for several years after patients have completed the trial treatment.
However, doctors involved in the design of the trial will present interim results at national and international conferences throughout the trial. Together, they will help shape the design of future myeloma clinical trials.

There is no mandatory requirement to inform patients who take part in clinical trials of the results, but patients are very welcome to seek or request results when they are available from their doctor or from Myeloma UK.

As well as the Myeloma XI trial, many other clinical trials are taking place in the UK and around the world, the results of which will also help to increase our understanding of myeloma.

For example, much research is ongoing into the biology and genetics of myeloma to determine the factors responsible for its onset and progression.

Researchers have so far identified subgroups of patients, each with specific genetic characteristics that are thought to be responsible for the variability amongst patients both in the nature and biology of their myeloma and in their response to treatment.

Much attention is currently focused on a better understanding of these genetic characteristics which will in turn, it is hoped, form the basis for more targeted drugs and more specific genetic diagnostic tests to be developed and tested.

Importantly, this information should set the scene for more personalised medicine strategies in the future, providing each patient with the best possible treatment for their myeloma.

For this type of research to be successful, it is increasingly recognised that there is a need to establish more myeloma-specific tissue banks. This enables samples from consenting patients to be collected for future trials. While patients may not benefit directly by donating their tissue samples (blood, bone marrow biopsy), they will be helping other myeloma patients in the future.
Key points about clinical trials

- Clinical trials are planned investigations in which patients take part. They are designed to test new treatments or compare different types of treatments.

- The purpose of clinical trials is to test whether or not a new treatment has a real benefit for patients compared to current standard treatments.

- Clinical trials are also carried out to find the best ways of using available treatments.

- Clinical trials are run according to a strict set of procedures called a protocol. These procedures and processes ensure that all patients in the trial are treated as safely as possible.

- If a patient decides to take part in a clinical trial, their doctor will ensure they are treated as safely and effectively as possible.

- Not all patients will be suitable for a clinical trial. Each trial will have eligibility criteria – a set of characteristics patients in the trial must have. These criteria are very important and help protect the safety of patients and ensure they are not exposed to unnecessary risks.

- It is always the patient’s decision to take part in a clinical trial. They should be given support and all relevant information about the trial, to enable them to make their decision.

- Choosing not to take part will not affect the standard of patients’ care, or their relationship with their doctor.

- Before taking part in a clinical trial, patients must sign an Informed Consent Form. For more information on informed consent, see page 21 of this Infoguide.

- If patients are taking part in a trial comparing two or more treatments, the treatment they receive will be decided randomly by a computer system. For more information on randomisation, see page 8 of this Infoguide.

- If patients decide to withdraw from the trial treatment at any point, all other treatment options available will be discussed. Their decision to withdraw should not affect their standard of care or their relationship with their doctor.
Questions for the doctor or nurse

It is common to have many questions, particularly when patients are recently diagnosed and are considering taking part in a clinical trial. The relationship patients have with their doctor and nurse should involve trust and collaboration and patients should feel comfortable asking questions about the clinical trial they have been asked to take part in.

It may be helpful for patients to write down any questions they have and give a copy to their doctor at the start of their consultation. They may wish to call the Myeloma Infoline to receive the free patient diary which has a ‘notes’ section where they can write down questions as they come to them.

Some questions patients may want to ask include:

- Why should I take part in this trial?
- How long will the trial last?
- How much extra time will it involve for me to take part in this trial?
- What are the benefits and risks of taking part?
- What will the treatment involve?
- Is this the best treatment for me?
- Are there any alternative treatment options?
- Where will my treatment be carried out?
- What are the side-effects of the treatments?
- How long might the side-effects last?
- Who do I contact if I have side-effects/symptoms to report?
• Who can I call in an emergency?
• Will treatment affect my chances of having children in the future?
• What will happen with my tissue samples?
• Will my details be kept confidential?
• Who is sponsoring this trial?
• Will the results of the trial be available for me to see?
• What will happen to me when the trial has finished?
Medical terms explained

**Apheresis:** A procedure in which stem cells are collected from the blood using a machine which separates them out, returning the remainder of the blood components to the patient/donor. As stem cells are within the white blood cell components, it is also sometimes referred to as leukapheresis.

**Autologous stem cell transplant:** A procedure in which a patient’s own stem cells are collected, stored and then given back following high-dose chemotherapy. This is the most common type of transplantation used in myeloma.

**Bisphosphonates:** A type of drug that binds to the surface of bone and protects against bone breakdown by cells that remove bone. They include sodium clodronate (Bonefos®), pamidronate (Aredia®) and zoledronic acid (Zometa®). In myeloma, they are used to treat myeloma bone disease and high levels of calcium in the blood (hypercalcaemia).

**Bone marrow:** The soft spongy tissue in the centre of the bones that produces white blood cells, red blood cells and platelets.

**CD34+ blood test:** A test which measures the amount of stem cells in the blood.

**Chemotherapy:** Treatment with potent/cytotoxic drugs intended to kill cancer cells. Chemotherapy can be injected into a vein (intravenous or IV) or swallowed as tablets (orally).

**Consolidation treatment:** Treatment given after initial treatment to further reduce the number of myeloma cells to achieve and sustain remission.

**DNA:** Deoxyribonucleic acid – the hereditary material that contains the genetic information used by all living organisms in order to function.
Eligibility criteria: Requirements that must be met for a patient to take part in a clinical trial. These help to protect the safety of patients and ensure they are not exposed to any unnecessary risks.

First-line treatment: First course of treatment given after diagnosis.

Glucocorticoids: A type of steroid hormone made by the adrenal glands which exert multiple actions in the body.

Granulocyte-colony stimulating factor: A growth factor which stimulates the bone marrow to make more stem cells.

Growth factor: A protein that stimulates the growth of cells.

High-dose therapy: High-dose chemotherapy which is given intravenously, usually via the central line, prior to giving back previously collected healthy stem cells as part of the transplantation process.

Histone deacetylase: An enzyme which alters the structure of DNA to enable the production of proteins to be turned on or off.

Histone deacetylase inhibitor: A drug that works by blocking the actions of enzymes called histone deacetylases from working, which leads to slowed cell growth and cell death.

Immunomodulatory drug: A drug that acts on the cells involved in the body’s immune system e.g. thalidomide and Revlimid.

Induction treatment: The initial treatment given prior to high-dose therapy and stem cell transplantation.

Initial treatment: The first treatment given to treat myeloma.

Intravenously: Into a vein, a way of injecting drugs.
Kyprolis (carfilzomib): A new drug being used to treat myeloma. Like Velcade® (bortezomib), Kyprolis belongs to a group of drugs known as proteasome inhibitors. However, Kyprolis has been developed to specifically target a different area of the proteasome to Velcade. This is thought to make Kyprolis possibly more effective and potentially cause fewer side-effects than Velcade. This is only used in version 6 of the trial protocol, as part of a four-drug initial treatment.

Maintenance treatment: The treatment given after chemotherapy or transplantation to prolong the period of response.

Melphalan: A type of chemotherapy drug used in the treatment of myeloma.

Mozobil (plerixafor): A drug used in combination with G-CSF to mobilise blood stem cells for collection prior to transplantation.

Paraprotein: An antibody-like protein produced by myeloma cells. It is found in blood and sometimes in urine. It is also called monoclonal protein, myeloma protein, M spike, M protein or M band.

Peripheral neuropathy: Damage to the peripheral nerves, particularly in the hands and feet causing pain, tingling and altered sensation.

Proteasome: A structure found in all cells that controls cell growth and function. It works by breaking down many different proteins that control the cell’s lifecycle.

Proteasome inhibitor: A drug that works by blocking the function of the proteasome, which can lead to slowed cell growth or cell death.

Protocol: An action plan for a clinical trial. The plan states what will be done in the trial and why. It outlines how many people will take part, what tests they will receive and how often and the treatment plan.

Radiotherapy: Treatment with X-rays, gamma rays or electrons to damage or kill malignant cells/tumours, and to treat localised pain.
Randomisation: A method used to prevent bias in research. Trial participants are assigned by chance to either the treatment or control group.

Relapsed: The point where myeloma returns or becomes more active after a period of remission or stable disease.

Revlimid: A new type of drug called an immunomodulatory drug which has been shown to be effective in treating myeloma. The way it works is not completely understood but it is thought to affect the way the immune system works. Revlimid is chemically similar to thalidomide and its prescription is subject to a strict risk management programme. Also known as lenalidomide.

RNA: Ribonucleic acid is the chemical molecule responsible for transferring the genetic information from DNA to the cell's protein-forming system.

Second-line treatment: Treatment given when the initial (first-line) treatment does not work or stops working.

Side-effects: Problems that occur when treatment affects healthy cells. Common side-effects of standard cancer treatments are fatigue, nausea, vomiting, decreased blood cell counts, hair thinning/loss and mouth sores.

Sodium clodronate: A type of bisphosphonate, also known as Bonefos®.

Standard treatment: The best treatment currently known for a cancer, based on results of past research.

Stem cell: The immature cells from which all blood cells are derived. Stem cells give rise to normal blood cell components, including red cells, white cells and platelets. They are normally located in the bone marrow and can be harvested for transplant.

Stem cell mobilisation: The process by which the number of stem cells in the bone marrow are increased, so that the cells ‘spill over’ into the blood stream and can be collected and stored.
Steroid: Hormonal substances which are naturally produced by the body. Those used in the treatment of myeloma are known as glucocorticoids. These steroids suppress inflammation and the immune system.

Thalidomide: A drug that has been found to be effective in treating myeloma. It is being used and studied at all stages of disease. This drug was originally used as a sedative and then as anti-sickness treatment but was withdrawn in the 1960s because of the birth defects it caused when taken during pregnancy. Its use is now subject to a strict risk management programme.

Third-line treatment: Treatment that is given when both initial (first-line) and subsequent (second-line treatment) has failed to work or when the myeloma becomes active again after two previous treatments.

Velcade: The first of a new type of cancer drugs called proteasome inhibitors. Velcade works by blocking the proteasome, causing cells to die. Also known as bortezomib.

Vorinostat: A new type of cancer drug known as a histone deacetylase inhibitor. Vorinostat works by stopping enzymes called histone deacetylases from working and preventing proteins needed for cell growth and survival from being made. This ultimately causes cells to die.

Zoledronic acid (formerly known as Zometa): A type of bisphosphonate used to treat myeloma bone disease.
Further information and useful organisations

United Kingdom

Blue Badge Scheme  www.gov.uk/government/collections/blue-badge-scheme
Helps those with severe mobility problems who have difficulty using public transport to park close to where they need to go.

British Association for Counselling and Psychotherapy (BACP)  www.bacp.co.uk
01455 883300 (General enquiries; Monday – Friday, 8.45am – 5pm)
BACP is a membership organisation that sets standards for therapeutic practice and provides information for therapists, clients of therapy and the general public. BACP aims to increase public understanding of the benefits of counselling and psychotherapy, raise awareness of what can be expected from the process of therapy and promote education and/or training for counsellors and psychotherapists.

British Kidney Patient Association  www.britishkidney-pa.co.uk
01420 541424 (Monday – Friday, 9am – 5pm)
Provides information and advice for patients with kidney disease, grants to help patients and families with kidney disease cover the costs of domestic bills, hospital travel, education and holidays, and financial support to kidney units throughout the UK to help improve kidney services and patient care.

British Red Cross  www.redcross.org.uk
0844 871 1111 (General enquiries; Monday – Friday, 9am – 5pm)
Volunteers assist with local services – including care in the home, transport and medical loans – to help those with health issues lead a full and independent life. They provide short-term loans of equipment at almost 1000 outlets in the UK. The Home from Hospital Service provides short-term practical assistance and support to help people settle back into their own homes. A Transport and Escort Service offers help to people who cannot get about easily or use ordinary transport.

Cancer Black Care  www.cancerblackcare.org.uk
020 8961 4151 (Monday – Friday, 9am – 5pm)
Provides a support service to ALL members of the community affected by cancer. We offer a safe, confidential, neutral place where service users, carers and families and friends can meet to support each others cultural and emotional needs.
Cancer Research UK www.cancerhelp.org.uk 0808 800 4040 (Nurse Information line; Monday – Friday, 9am – 5pm)
CancerHelp UK is the patient information website of Cancer Research UK. It provides a free information service about cancer and cancer care for patients and their families.

Carer's Allowance Unit www.gov.uk/carers-allowance-unit 0845 608 4321 (Monday – Thursday 8.30am – 5pm; Friday 8.30am – 4.30pm)
General information about the carer’s allowance, and how to make a claim.

Carers UK www.carersuk.org 0808 808 7777 (Monday – Friday 10am – 4pm)
Carers UK provides information, advice and support for carers. It produces a directory of national and local carer organisations and can show you where to get help in your area.

Carers Trust www.carers.org www.youngcarers.net 0844 800 4361 (Monday – Friday, 9am – 5pm)
Formed by the merger of The Princess Royal Trust for Carers and Crossroads Care in April 2012. It works to improve support, services and recognition for anyone living with the challenges of caring, unpaid, for a family member or friend who is ill, frail, disabled or has mental health or addiction problems.

Citizens Advice Bureau (CAB) www.citizensadvice.org.uk 0844 4111 444 – from England (Monday – Friday 9am – 5pm) 0844 4772 020 – from Wales (Monday – Friday 9am – 5pm)
Citizens Advice Bureau offers advice about debt and consumer issues, benefits, housing, legal matters and employment. It provides assistance with claiming welfare benefits, including practical help with filling out benefit application forms.

Cruse Bereavement Care www.cruse.org.uk 0844 477 9400 (Monday – Friday, 9.30am – 5pm)
Cruse Bereavement Care exists to promote the wellbeing of bereaved people and to enable anyone bereaved to understand their grief and cope with their loss. They provide face-to-face and telephone support, counselling and information.
Depression Alliance  www.depressionalliance.org
0845 123 2320 (Information pack request line only)
Provides information, support and understanding for those affected by depression and coordinates a network of self-help groups throughout the UK. They also produce a wide range of publications covering various aspects of depression.

DIAL UK  www.scope.org.uk
0808 800 3333 (Monday – Friday, 9am – 5pm)
A national organisation for local disability information and advice services run by and for disabled people. Provides information and advice on all aspects of living with a disability, including welfare benefits, transport, mobility and equipment.

Disability Benefits Helpline  08457 123456
Phone the Disability Benefits Helpline for advice about which benefits you may be entitled to.

Disability Rights UK  www.disabilityrightsuk.org
020 7250 3222 (Monday – Friday, 9am – 12.30pm; 1.30pm – 4pm)
0300 555 1525 (Independent Living Advice Line; Monday & Thursday 9am – 1pm)
Disability Rights UK produce high quality information, products and services developed by and for disabled people. They partner with the private and public sector, with the aim of improving business practices.

Directgov  www.direct.gov.uk
A government website which provides information about a wide range of public services including benefits such as Attendance Allowance, Disability Living Allowance and Carer’s Allowance.

Financial Conduct Authority  www.fca.org.uk
Consumer helpline 0800 111 6768
We regulate the financial services industry in the UK. Our aim is to protect consumers, ensure our industry remains stable and promote healthy competition between financial services providers. We have rule-making, investigative and enforcement powers that we use to protect and regulate the financial services industry. We are fair and principled in our approach to regulation.
Finding a job – GOV.UK www.gov.uk/browse/working/finding-job
Information and claims service for income support, incapacity benefit, job seekers allowance and employment and support allowance.

Help the Hospices www.helpthehospices.org.uk
020 7520 8200 (Monday – Friday, 9am – 5pm)
Help the Hospices provides information to health professionals and the general public about hospice and palliative care services in the UK. It’s online and telephone service can help you find a local hospice.

Help with Health Costs www.nhs.uk/Healthcosts
Help with Health Costs gives information about prescription charges and getting help with health costs. It also issues exemption from health costs certificates, and prescription pre-payment certificates.

Independent Financial Advice Promotion (IFAP) www.unbiased.co.uk
IFAP is the industry body responsible for promoting independent financial advice in the UK. It provides a UK-wide list of authorised financial advisers on its website. IFAP also produces a wide range of publications covering various aspects of financial management including mortgages, savings, investments and pensions.

Institute for Complementary and Natural Medicine (ICNM) www.icnm.org.uk
0207 922 7980 (Monday – Friday, 10am – 4pm)
The Institute for Complementary and Natural Medicine (ICNM) provides the public with information about all aspects of complementary medicine. It also administers the British Register of Complementary Practitioners, providing details of local registered practitioners of various complementary therapies.

Leukaemia CARE www.leukaemiacare.org.uk
0808 8010 444 (24 hours a day, 7 days a week)
Exists to provide care and support to all those whose lives have been affected by leukaemia, lymphoma, myeloma and the allied blood disorders. Leukaemia CARE also offers discrentional financial assistance and caravan holidays in the UK.
Leukaemia & Lymphoma Research  www.leukaemialymphomaresearch.org.uk
020 7504 2200 (Monday – Friday, 9am – 5pm)
Funds research into leukaemia and related blood disorders including lymphoma and myeloma. It also provides free patient information booklets with accessible and accurate information on blood cancers and the related disorders.

Macmillan Cancer Support Benefits Advice
www.macmillan.org.uk/HowWeCanHelp/FinancialSupport/BenefitsAdvisers/
MacBenefitsAdvisers.aspex
0800 500 800 (Monday – Friday, 10am – 5pm)
Macmillan Cancer Support offers information about how to access benefits and other kinds of financial support.

Macmillan Cancer Support  www.macmillan.org.uk
0808 808 0000 Macmillan Support Line; Monday – Friday, 9am – 9pm
If you are deaf or hard of hearing you can use the textphone service on 0808 808 0121.

Marie Curie Cancer Care  www.mariecurie.org.uk
0800 716 146 (Monday – Friday, 9am – 5pm)
Marie Curie provides specialist palliative nurses and has nine Marie Curie Centres providing free respite and hospice care throughout the UK.

MedicAlert®  www.medicalert.org.uk
01908 951045 (Monday – Friday, 9am – 5pm)
MedicAlert is a non-profit charity that provides a life-saving identification system for individuals with hidden medical conditions.

Medical Research Council (MRC)  www.mrc.ac.uk
01793 416200 (Head office switchboard; Monday – Friday, 9am – 5pm)
The MRC promotes research into all areas of medical and related science.
National Amyloidosis Centre (NAC)  www.ucl.ac.uk/amyloidosis/nac
020 7433 2725 (General enquiries; Monday – Friday, 9am – 5pm)
Based at the Royal Free and University College Medical School, London, the NAC is the only centre in the UK specialising in amyloidosis. The centre has state of the art clinical and research facilities and a team of highly qualified clinical, research and support staff.

National Cancer Research Institute (NCRI)  www.ncri.org.uk
020 3469 8460 (Monday – Friday, 9am – 5pm)
The National Cancer Research Institute is a partnership of health departments, the Medical Research Council and major cancer charities which aims to develop common plans for cancer research.

National Debtline  www.nationaldebtline.co.uk
0808 808 4000 (Monday – Friday, 9am – 9pm; Saturday 9.30am – 1pm)
Offers free, confidential and independent advice on how to deal with debt problems.

National Institute for Health and Care Excellence  www.nice.org.uk
0845 003 7780 (Monday – Friday, 9am – 5pm)
NICE is an independent organisation responsible for providing national guidance on promoting good health and preventing and treating ill health. NICE produces guidance on health technologies (the use of new and existing medicines, treatments and procedures) and clinical practice (guidance on the appropriate treatment and care of people with specific diseases) within the NHS.

National Kidney Federation (NKF)  www.kidney.org.uk
0845 6010 209 (Monday – Friday, 9am – 5pm)
The National Kidney Federation provides information about kidney disease and dialysis, and promotes best practice in renal medicine.
NHS helplines

NHS 111 is a free-to-call single non-emergency number medical helpline operating in England and Scotland. The service is part of each country’s National Health Service and has replaced the telephone triage and advice services provided by NHS Direct, NHS24 and local GP out-of-hours services. The transition was completed in England during February 2014 with Scotland following during April 2014.

The service is available 24 hours a day, every day of the year and is intended for ‘urgent but not life-threatening’ health issues and complements the long-established 999 emergency telephone number for more serious matters, although 111 operators are able to dispatch ambulances when appropriate using the NHS Pathways triage system.

NHS Direct Wales continues to operate via 0845 4647, but it is intended the 111 service will be offered from some point in 2015.

OvercomeDepression www.overcomedepression.co.uk

OvercomeDepression aims to offer a unique reference point for information and practical advice on depression.

Pain Association Scotland www.chronicpaininfo.org

0800 783 6059 (Monday – Friday, 8.00am – 4.30pm)

Pain Association Scotland offers support to people with chronic pain and organises pain management support groups across Scotland.

Pain Concern www.painconcern.org.uk

0300 123 0789 (Monday – Friday, 10am – 4pm)

Pain Concern provides a range of information about self-help and managing pain. Its helpline offers information, support and a listening ear.

Penny Brohn Cancer Care www.pennybrohncancercare.org

0845 123 2310 (Monday – Friday, 9.30am – 5pm)

Based in Bristol, Penny Brohn Cancer Care offers support to anyone affected by cancer. They offer a unique combination of physical, emotional and spiritual support designed to help you at any stage of your illness.
The Pensions Advisory Service www.pensionsadvisoryservice.org.uk
0845 601 2923 (Monday – Friday, 9am – 5pm)
The Pensions Advisory Service is an independent non-profit organisation that provides free information, advice and guidance on a spectrum of pensions covering state, company, personal and stakeholder schemes.

The Pension Service www.thepensionservice.gov.uk
0845 6060 265 (Pension helpline; Monday – Friday, 8am – 8pm)
The Pension Service helps with state pension eligibility, claims and payments.

Relate www.relate.org.uk
0300 100 1234 (Monday – Thursday, 8am – 10pm; Friday, 8am – 6pm; Saturday, 8am – 4pm)
Offers a counselling service for couples or individuals experiencing difficulties in their relationship. Provides support face-to-face, by phone and on its website.

Samaritans www.samaritans.org
08457 90 90 90 (24 hours a day, 7 days a week)
Samaritans provides confidential non-judgemental emotional support, 24 hours a day for people who are experiencing feelings of distress or despair. It offers services by telephone, email, letter and face to face.

SSAFA (Soldiers, Sailors, Airmen and Families Association) www.ssafa.org.uk
0800 731 4880 (Forcesline helpline; Monday – Friday 10.30am – 7.30pm)
A national charity committed to supporting those who serve or have served (even for just one day) in our Armed Forces. It offers a Confidential Support Line, financial assistance, help in organising and funding home adaptations or special equipment and practical/emotional support for those who are lonely, bereaved or ill.

Tenovus Cancer Information Centre www.tenovus.org.uk
0808 808 1010 (Monday – Friday, 9am – 5pm)
Tenovus is a charity committed to the control of cancer through research, education, counselling and patient care. Its helpline offers information and support to those affected by cancer.
UK Myeloma Forum www.ukmf.org.uk
An organisation of people professionally engaged in the field of myeloma who are working to improve the outlook for patients with myeloma and related disorders. On behalf of the British Committee for Standards in Haematology, UKMF has produced guidelines on the diagnosis, treatment and management of myeloma.

Northern Ireland

Cancer Focus Northern Ireland www.cancerfocusni.org
0800 783 3339 (Monday – Friday, 9am – 5pm)
Cancer Focus Northern Ireland offers information, support and counselling to people affected by cancer in Northern Ireland. Its helpline is staffed by specially trained nurses with experience in cancer care.

Ireland

ACCORD www.accord.ie
01 505 3112
Caring for marriage and relationships. It is the largest marriage-care agency in Ireland.

Association of Registered Complementary Health Therapists of Ireland 053 938 3734 www.irishtherapists.ie
It acts as an umbrella association in order to promote better awareness of complementary health medicine.

Care www.carers.ie
01 679 3188
Carers provide practical information and guidance for people who are caring for someone who has been diagnosed with a life-threatening illness in Ireland.

Chronic Pain Ireland www.chronicpain.ie
01 804 7567 (Monday – Thursday, 9.30am – 5pm)
Provides information and support to those living with chronic pain, their families and friends.
Citizens Information  www.citizensinformation.ie
0761 07 4000 (Monday – Friday, 9am – 8pm)
Provides information on public services and entitlements in Ireland.

Irish Cancer Society  www.cancer.ie
1 800 200 700 (Monday – Thursday, 9am – 7pm, Friday, 9am – 5pm)
From the UK dial 00 353 1 2310 500
Provides advice, support and information to people in Ireland affected by cancer. It also publishes a range of patient information, including a booklet on myeloma.

The Irish Hospice Foundation  www.hospice-foundation.ie
01 679 3188 (Monday – Friday, 9am – 1pm, Monday – Thursday, 2pm – 5.30pm, Friday 2pm – 5pm)
Works independently and in partnership with the statutory, voluntary and professional bodies with hospice and palliative care in Ireland.

Ireland out of hours
For Ireland out of hours contacts visit: www.hse.ie/eng/services/list/3/outofhours

MyMyeloma  www.mymyeloma.ie
087 233 7797
Dedicated Irish myeloma website for patients, family members and those with an interest in myeloma.

Overseas

Myeloma Patients Europe (MPE)  www.myelomapatientseurope.org
MPE was formed following a merger between the European Myeloma Platform and Myeloma Euronet. It is a non-profit organisation and acts as an umbrella organisation for existing local and national myeloma associations and its members come from nearly 30 countries. MPE is dedicated to raising awareness of myeloma.

Multiple Myeloma Research Foundation (MMRF)  www.multiplemyeloma.org
00 1 203 6520219
The MMRF is a US-based private funder of worldwide myeloma-specific research. It provides information about myeloma treatments and international clinical studies.
About Myeloma UK

Myeloma UK is the only organisation in the UK dealing exclusively with myeloma, a bone marrow cancer for which there is no cure, but many very effective treatments. Our broad and innovative range of services cover every aspect of myeloma from providing information and support, to improving standards of treatment and care through research, education, campaigning and raising awareness.

At Myeloma UK we are passionate and dedicated about what we do and have a relentless commitment to achieving our goals. The organisation receives no government funding and rely almost entirely on voluntary donations and fundraising activities.

With Myeloma UK you can...

- Call our Myeloma Infoline on 0800 980 3332 or 1800 937 773 from Ireland for information, practical advice, emotional support and a listening ear
- Get free Infopacks, Infoguides and Infosheets about myeloma
- Learn about myeloma from experts and meet others affected by myeloma by attending Patient and Family Myeloma Infodays
- Subscribe to our quarterly magazine Myeloma Matters
- Join a Myeloma Support Group
- Get the latest news on research breakthroughs, health service developments and share experiences with other myeloma patients and their families on our website www.myeloma.org.uk
Other information and support available from Myeloma UK

Infopacks
Infopack for newly diagnosed myeloma patients

Essential Guides
Myeloma – Your Essential Guide
Living with myeloma – Your Essential Guide

Infoguides
Infoguide topics include:
Balloon Kyphoplasty
Caring for someone with myeloma
Clinical studies
Cyclophosphamide, thalidomide and dexamethasone (CTD)
Fatigue
High-Dose Therapy & Autologous Stem Cell Transplantation
Melphalan, Prednisolone and Thalidomide (MPT)
Myeloma Bone Disease and Bisphosphonates
Myeloma and the kidney
Pain and myeloma
Revlimid® and myeloma
Serum Free Light Chain Assay
Velcade® and myeloma

Leaflets
Myeloma – An Introduction
About Myeloma UK
Myeloma UK – Publications list

Infosheets
Infosheet topics include: Constipation, Copayments, Diet and nutrition, Erythropoietin, Fatigue, Growth factors, Managing your finances (benefits and general), MGUS, Mouthcare, Osteonecrosis of the jaw, Peripheral neuropathy, Percutaneous Vertebroplasty, Plasma Cell Leukaemia, Plasmacytoma, Plasmapheresis, Prescription charges, Radiotherapy, Setting up a Support Group, Smouldering myeloma, Steroids, Support Groups, Travel insurance, Travelling.
Horizons Infosheet Series
These provide information on a number of treatments and procedures that are currently in the final stages of research or development and which are showing a great deal of promise. Current Horizons Infosheets available: Bendamustine, Denosumab, Daratumumab, Elotuzumab, Ixazomib, Kyprolis® (carfilzomib), Panobinostat, Imnovid® (pomalidomide).

Other resources

Children’s book about myeloma
Kelsey and the Yellow Kite.

Myeloma A – Z
A booklet which explains key glossary terms relating to myeloma.

Patient diary
This diary helps patients keep a track of hospital appointments and key test results in a practical, simple way. The diary (A5 in size) contains 11 sections which are neatly divided and tabbed for ease of reference as follows: Your myeloma diary, Appointments, Blood tests and results, Treatment records, Complementary therapies record, Symptoms and side-effects record, Questions to ask your doctor/nurse, Key myeloma terms, Further information and useful organisations, About Myeloma UK and Your notes.
We need your support

Thanks to our generous supporters we are able to provide information and services to patients and their loved ones, 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 donation** – online at www.myeloma.org.uk/donate, over the phone 0131 557 3332 or by posting a cheque payable to Myeloma UK, Broughton House, 31 Dunedin Street, Edinburgh EH7 4JG

- **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. However you decide to raise funds, our Fundraising Team is here to support you. Contact us on 0131 557 3332 or email fundraising@myeloma.org.uk

- **Leaving a legacy** – gifts from wills are an important source of income for Myeloma UK and will 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
Call our Myeloma Infoline on 0800 980 3332