

# Daratumumab (Darzalex<sup>®</sup>)

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**This Horizons Infosheet contains information on daratumumab (also known as Darzalex), a drug being investigated for the treatment of myeloma.**

The Horizons Infosheet series provides information relating to novel drugs and treatment strategies that are currently being investigated for the treatment of myeloma. The series also aims to highlight the considerable amount of research currently taking place in the field of myeloma.

The drugs and treatment strategies described in the

Horizons Infosheets may not be licensed and/or approved for use in myeloma. You may, however, be able to access them as part of a clinical trial.

## **What is daratumumab?**

Daratumumab is a new drug being investigated for the treatment of myeloma. Daratumumab is a monoclonal antibody which attaches

specifically to a protein that is present on the surface of myeloma cells.

### What is a monoclonal antibody?

Monoclonal antibodies are a class of drug being investigated in the treatment of myeloma.

Monoclonal antibodies are made in the laboratory to mimic the antibodies that your own immune system produces in response to foreign organisms (such as bacteria) that enter the body. 'Monoclonal' means all one type. This means that each group of monoclonal antibodies is made up of identical copies of one type of antibody.

Monoclonal antibodies are designed to recognise and attach to specific proteins on the surface of cancer cells. Each group of monoclonal antibody recognises one particular protein.

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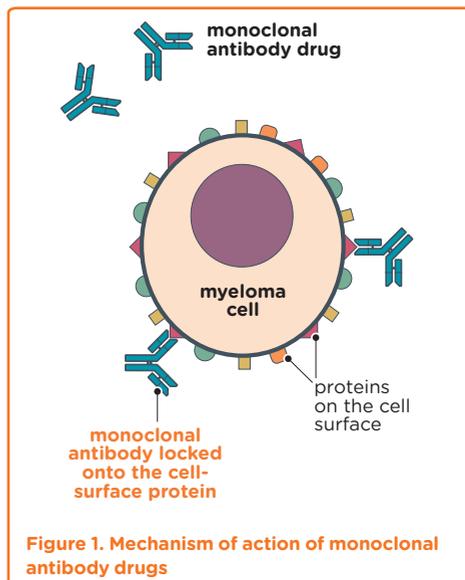
**For more information see the [Immunotherapy Infosheet](#) from Myeloma UK**

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### How does daratumumab work?

Myeloma cells produce a protein called CD38 which is present on the cell surface. Daratumumab attaches to the CD38 protein

found on the surface of myeloma cells, enabling the immune system to target and kill it (Figure 1).



**Figure 1. Mechanism of action of monoclonal antibody drugs**

### How is daratumumab given?

Daratumumab is currently given by intravenous infusion (into a vein) over a number of hours, although subcutaneous (under the skin) delivery is also being explored in clinical trials (see page 5). The recommended dose when used as intravenous monotherapy (used on its own and not in combination with other drugs) is 16 milligram per kilogram (mg/kg) which is given once a week for the first 8 weeks. From week 9 to week 24,

daratumumab is given every 2 weeks, and then every 4 weeks. Treatment continues for as long as the patient benefits from it.

Daratumumab has shown to be effective as a monotherapy. It is also being trialled in combination with other antimyeloma treatments such as dexamethasone, bortezomib (Velcade®) and lenalidomide (Revlimid®).

Trials are being carried out in both newly diagnosed and relapsed and/or refractory patients.

### **What evidence exists to support the use of daratumumab?**

The Phase III CASTOR trial compared daratumumab in combination with bortezomib and dexamethasone to bortezomib and dexamethasone only in 500 relapsed and/or refractory myeloma patients. Results have shown that the number of patients responding to treatment increased when daratumumab was added to bortezomib and dexamethasone (from 63% to 83%). Further evaluation found that high-risk patients (with a more active or difficult to treat myeloma) also responded well to the addition of

daratumumab (82% responding compared to 62% given bortezomib and dexamethasone only).

Furthermore, the addition of daratumumab was found to reduce the risk of disease progression (the length of time following treatment before myeloma returns and further treatment is required) by 61% when added to bortezomib and dexamethasone.

The Phase III POLLUX trial is investigating daratumumab, lenalidomide and dexamethasone compared to lenalidomide and dexamethasone only in relapsed and/or refractory patients. By adding daratumumab to lenalidomide and dexamethasone, the number of patients responding to treatment increased (from 76% to 93%) and also doubled the rate of complete response (where the response to treatment results in less than 5% plasma cells in the bone marrow) compared to lenalidomide and dexamethasone alone.

Significantly more high-risk patients responded with the addition of daratumumab (91% compared to 69% with lenalidomide and dexamethasone only). Initial findings also show a

3% reduction in the risk of disease progression when patients were treated with daratumumab, lenalidomide and dexamethasone compared to lenalidomide and dexamethasone alone.

### **What are the possible known side-effects of daratumumab?**

The most commonly observed side-effect of daratumumab is an 'infusion reaction', which most often occurs within three to four hours of receiving the intravenous infusion. This can include fever, chills, cough, nausea, changes in blood pressure, flushing, rash and fatigue. An infusion reaction is typically more likely to occur with the first infusion rather than second or subsequent.

Other side-effects reported include: low white blood cell levels (leukopenia); low platelet levels (thrombocytopenia); low red blood cell levels (anaemia) and elevated liver enzymes.

### **Is daratumumab currently available in any UK clinical trials?**

For an up-to-date list of UK clinical trials involving daratumumab, visit the **Myeloma Trial Finder** on [www.myeloma.org.uk](http://www.myeloma.org.uk)

To be enrolled on a clinical trial, patients have to meet certain conditions known as eligibility criteria. You should speak to your doctor in the first instance if you are interested in taking part in a trial.

### **Availability of daratumumab in the UK**

Before a drug can be widely used, it must first be licensed as a safe and effective treatment. This is usually done by regulatory authorities at a European level and involves a review of evidence from large-scale clinical trials.

Normally, the licensed drug must then be approved by a UK drug appraisal body before it can be routinely prescribed by NHS doctors. The drug appraisal process differs from licensing - it compares how effective the newly licensed drug is to existing drugs already in use on the NHS and decides whether it offers the NHS good value for money. The main body responsible for carrying out drug appraisals in England and Wales is the National Institute for Health and Care Excellence (NICE). NICE recommendations are usually adopted in Northern Ireland. Scotland's drug appraisal

body is the Scottish Medicines Consortium (SMC).

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**For more information see the [Health Technology Assessment Infosheet](#) from [Myeloma UK](#)**

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Daratumumab has been granted a licence by the European Medicines Agency (EMA) for use across Europe as both a monotherapy and also in combination with lenalidomide and dexamethasone **or** bortezomib and dexamethasone in relapsed and/or refractory patients.

In October 2017 the SMC approved the use of daratumumab monotherapy in Scotland as a fourth line treatment.

In January 2018 NICE approved daratumumab monotherapy for English and Welsh patients as a fourth line treatment, through a government fund called the Cancer Drugs Fund (CDF). Under the CDF, NICE can issue a conditional 'yes' to promising drugs about which there is still some uncertainty regarding clinical effectiveness. Under this agreement, there is a two year period where more data on the effectiveness of the drug is collected. NICE then make a final

decision as to whether it should be approved for routine use.

In Northern Ireland the Department of Health, Social Services and Public Safety usually reviews NICE guidance within three months of publication. However, there is currently a lack of clarity about the process for providing access in Northern Ireland to drugs approved via the CDF. Now that this approval has been granted via the CDF, Myeloma UK will be working with the DHSPSS to clarify their intentions in relation to funding daratumumab for patients in Northern Ireland.

NICE is also currently appraising the combination of daratumumab, bortezomib and dexamethasone.

### **Future directions**

One of the challenges of giving daratumumab is that the intravenous infusion takes a long time – in particular, the first dose can take several hours to administer. The phase I PAVO trial investigated a subcutaneous (under the skin) method of administering daratumumab, in a matter of minutes, with promising results: subcutaneous daratumumab was found

to be tolerable with fewer occurrences of infusion reactions when compared to giving it intravenously. Further research into this method of administration is ongoing.

Daratumumab continues to be studied in different patient groups and in different treatment combinations. These trials will provide information about the safest and most effective way to use daratumumab in myeloma.

### **About this Horizons Infosheet**

The information in this Horizons Infosheet is not meant to replace the advice of your medical team. They are the people to ask if you have questions about your individual situation. All Myeloma UK publications are extensively reviewed by patients and healthcare professionals prior to publication.

For a list of references used to develop our resources, visit

**[www.myeloma.org.uk/  
references](http://www.myeloma.org.uk/references)**

To provide feedback about this publication, email

**[myelomauk@myeloma.org.uk](mailto:myelomauk@myeloma.org.uk)**

## Other information available from Myeloma UK

Myeloma UK has a range of publications available covering all areas of myeloma, its treatment and management.

To order your free copies or to talk to one of our Myeloma Information Specialists about any aspect of myeloma, call our Myeloma UK Infoline on **0800 980 3332** or **1800 937 773** from Ireland.

The Infoline is open from Monday to Friday, 9am to 5pm and is free to phone from anywhere in the UK and Ireland.

Information and support about myeloma is also available around the clock at **[www.myeloma.org.uk](http://www.myeloma.org.uk)**

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