



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## Darzalex (*daratumumab*)

An overview of Darzalex and why it is authorised in the EU

### What is Darzalex and what is it used for?

Darzalex is a cancer medicine used to treat adults with multiple myeloma (a cancer of the bone marrow). In patients with newly diagnosed multiple myeloma it is used:

- in combination with the medicines lenalidomide and dexamethasone or with bortezomib, melphalan and prednisone in patients who cannot have autologous stem cell transplant (a transplant of the patient's own blood-producing cells). Bortezomib, lenalidomide and melphalan are used for treating multiple myeloma and dexamethasone and prednisone suppress the immune system;
- in combination with bortezomib, thalidomide (another medicine used to treat multiple myeloma), and dexamethasone, in patients who can have autologous stem cell transplant.

In patients with previously treated multiple myeloma it is used:

- in combination with dexamethasone plus either lenalidomide or bortezomib;
- on its own when the disease has come back after treatment with cancer medicines (including medicines known as proteasome inhibitors) and immunomodulatory medicines (that act on the immune system), or when the disease has not improved with these medicines.

Multiple myeloma is rare and Darzalex was designated an 'orphan medicine' (a medicine used in rare diseases) on 17 July 2013. Further information on the orphan designation can be found here:

[ema.europa.eu/Find medicine/Human medicines/Rare disease designation](http://ema.europa.eu/Find%20medicine/Human%20medicines/Rare%20disease%20designation)

Darzalex contains the active substance daratumumab.

### How is Darzalex used?

Darzalex can only be obtained with a prescription and should be given by a healthcare professional in a setting where severe reactions can be quickly treated.

It is given by infusion (drip) into a vein or by injection under the skin. The recommended dose depends on the way the medicine is given. How often Darzalex is given depends on which other medicines are

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being given with it. Treatment usually starts with one dose of Darzalex once a week. Before and after treatment with Darzalex, patients are given medicines to reduce the risk of reactions. If the patient has severe infusion-related reactions, the doctor may slow down the infusion rate or stop treatment.

For more information about using Darzalex, see the package leaflet or contact your doctor or pharmacist.

## **How does Darzalex work?**

The active substance in Darzalex, daratumumab, is a monoclonal antibody (a type of protein) that has been designed to attach to the protein CD38, which is found in high amounts on multiple myeloma cells. By attaching to CD38 on the multiple myeloma cells, daratumumab activates the immune system to kill the cancer cells.

## **What benefits of Darzalex have been shown in studies?**

### **Previously treated multiple myeloma**

Darzalex on its own was investigated in two main studies involving a total of 196 multiple myeloma patients whose disease came back after, or did not respond to, at least two previous treatments including a proteasome inhibitor and an immunomodulatory medicine. The main measure of effectiveness was the proportion of patients who responded to treatment (as measured by the disappearance of, or at least a 50% reduction in, a protein found in multiple myeloma cells). Around 29% of the patients receiving Darzalex at a dose of 16 mg/kg (31 out of 106 patients) responded to treatment in one study and 36% (15 out of 42 patients) in the second study. In these studies Darzalex was not compared with any other treatment.

Darzalex, given together with dexamethasone and either lenalidomide or bortezomib, was investigated in two further main studies involving patients whose multiple myeloma came back after treatment with other medicines or did not respond to the treatment. The main measure of effectiveness was how long patients lived without their disease getting worse. In the first of these studies involving 569 patients, 78% of patients receiving Darzalex and dexamethasone plus lenalidomide for 18 months lived without their disease getting worse compared with 52% of those receiving dexamethasone plus lenalidomide. In the second study involving 498 patients, 61% of patients receiving Darzalex and dexamethasone plus bortezomib for 12 months lived without their disease getting worse compared with 27% of those receiving dexamethasone plus bortezomib.

Another study, involving 522 patients with multiple myeloma that came back after previous treatment or had not responded, showed that Darzalex by injection under the skin was no less effective in treating the condition than Darzalex by infusion into a vein; the disease responded in 41% (108 of 263) of patients given the injection and 37% (96 of 259) of patients given the infusion.

### **Newly diagnosed multiple myeloma**

Darzalex given together with dexamethasone and lenalidomide was compared with dexamethasone plus lenalidomide in patients with newly diagnosed multiple myeloma who could not have an autologous stem cell transplant. The study involved 737 patients and 70% of patients receiving Darzalex and dexamethasone plus lenalidomide lived for 36 months without their disease getting worse compared with 39% of those receiving dexamethasone plus lenalidomide.

Darzalex in combination with bortezomib, melphalan and prednisone was compared with bortezomib, melphalan and prednisone in a study involving 706 patients with newly diagnosed multiple myeloma who could not have autologous stem cell transplantation. After about 28 months of starting the study,

70% (246 out of 350) of patients treated with Darzalex in combination with the other 3 medicines were alive with no worsening of their disease compared with 49% (174 out of 356) of patients treated with bortezomib, melphalan and prednisone.

Darzalex has also been studied in patients who could have autologous stem cell transplantation. In the study, which involved 1,085 patients, Darzalex combined with bortezomib, thalidomide and dexamethasone was compared with a combination of bortezomib, thalidomide and dexamethasone without Darzalex, both given for 4 treatment cycles before transplantation and 2 cycles afterwards. After 100 days following transplantation, all signs of the myeloma were absent in around 29% of patients given the Darzalex combination and 20% of those given bortezomib, thalidomide and dexamethasone alone.

## **What are the risks associated with Darzalex?**

The most common side effects with Darzalex (which may affect at least 1 in 5 patients) are infusion reactions, tiredness, weakness, fever, nausea (feeling sick), diarrhoea, constipation, peripheral oedema (swelling of the ankles and feet), cough, upper respiratory tract infections (such as nose and throat infections), difficulty breathing, neutropenia (low levels of neutrophils, a type of white blood cell), anaemia (low red blood cell counts), thrombocytopenia (low blood platelet counts) and peripheral sensory neuropathy (damage to the nerves in the arms and legs).

Serious side effects are pneumonia (infection of the lungs), bronchitis (inflammation of the airways in the lungs), upper respiratory tract infection, pulmonary oedema (fluid build-up in the lungs), sepsis (blood poisoning), flu, fever, dehydration, diarrhoea and atrial fibrillation (irregular rapid contractions of the upper chambers of the heart).

For the full list of side effects and restrictions with Darzalex, see the package leaflet.

## **Why is Darzalex authorised in the EU?**

The European Medicines Agency decided that Darzalex's benefits are greater than its risks and it can be authorised for use in the EU. Darzalex on its own was effective at treating multiple myeloma in patients whose disease had progressed despite at least two other medicines. Darzalex used together with dexamethasone plus either lenalidomide or bortezomib has also been found effective in patients who had received other treatment for multiple myeloma. Darzalex used with lenalidomide and dexamethasone or with bortezomib, melphalan and prednisone was effective at treating patients with newly diagnosed multiple myeloma who cannot have autologous stem cell transplantation; combination with bortezomib, thalidomide and dexamethasone was of benefit in patients who can have such transplantation. Patients with multiple myeloma had limited treatment options and Darzalex, which works in a different way to existing treatments, represented an alternative. Darzalex's side effects are considered acceptable and manageable.

Darzalex was originally given 'conditional authorisation' because there was more evidence to come about the medicine. As the company has provided the additional information necessary, the authorisation has been switched to full approval.

## **What measures are being taken to ensure the safe and effective use of Darzalex?**

The company that markets Darzalex will provide educational material to all healthcare professionals expected to use the medicine, to inform them that the medicine can affect the result of a blood test

(indirect Coombs test) used to determine suitability for blood transfusions. Patients who are prescribed Darzalex will be provided with a patient alert card with similar information.

Recommendations and precautions to be followed by healthcare professionals and patients for the safe and effective use of Darzalex have also been included in the summary of product characteristics and the package leaflet.

As for all medicines, data on the use of Darzalex are continuously monitored. Side effects reported with Darzalex are carefully evaluated and any necessary action taken to protect patients.

### **Other information about Darzalex**

Darzalex received a conditional marketing authorisation valid throughout the EU on 20 May 2016. This was switched to a full marketing authorisation on 28 April 2017.

Further information on Darzalex can be found on the Agency's website:  
[ema.europa.eu/medicines/human/EPAR/darzalex](http://ema.europa.eu/medicines/human/EPAR/darzalex) .

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