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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). It is used:

- in combination with the medicines bortezomib, melphalan and prednisone in patients with newly diagnosed multiple myeloma who are not eligible for autologous stem cell transplant (a transplant of the patient's own blood-producing cells). Bortezomib and melphalan are used for treating multiple myeloma and prednisone suppresses the immune system;
- 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;
- in combination with dexamethasone (a medicine that suppresses the immune system) plus either lenalidomide or bortezomib in patients who have previously received other treatment for the disease. Lenalidomide and bortezomib are medicines used for treating multiple myeloma.

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

Darzalex contains the active substance daratumumab.

How is Darzalex used?

Darzalex is given by infusion (drip) into a vein. The recommended dose is 16 mg per kilogram body weight.

For newly diagnosed multiple myeloma, Darzalex is given once a week for 6 doses, then every 3 weeks for 16 doses then every 4 weeks for as long as the patient benefits from it.

In patients whose disease has not improved or has come back after treatment with other medicines, Darzalex is given once a week for 8 doses, then every 2 weeks for 8 doses then every 4 weeks for as

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long as the patient benefits from it. If Darzalex is given with bortezomib, it is given once a week for the first 9 weeks then every 3 weeks for 5 doses and then every 4 weeks.

Before and after the infusion of Darzalex, patients are given medicines to reduce the risk of infusion-related reactions. The doctor may reduce the infusion rate or stop treatment in case of severe infusion-related reactions.

Darzalex can only be obtained with a prescription and should be given by a healthcare professional in a place where facilities for resuscitating patients are readily available. For more information about using Darzalex, see the package leaflet or contact your doctor.

How does Darzalex work?

The active substance in Darzalex, daratumumab, is a monoclonal antibody (a type of protein) that has been designed to recognise and 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?

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 completely or partially 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 completely or partially 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 (progression-free survival). 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.

In a study with 706 patients with newly diagnosed multiple myeloma who could not have autologous stem cell transplantation, Darzalex in combination with bortezomib, melphalan and prednisone was compared with bortezomib, melphalan and prednisone. 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.

What are the risks associated with Darzalex?

The most common side effects with Darzalex (which may affect around 1 in 2 people) are infusion-related reactions such as breathing problems, cough, runny or blocked nose, throat irritation, nausea (feeling sick), vomiting, and chills. Other frequent side effects (affecting at least 1 in 5 patients) are tiredness, fever, nausea (feeling sick), diarrhoea, muscle spasm, upper respiratory tract infections

(such as nose and throat infections), 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). 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 bortezomib, melphalan and prednisone was effective at treating patients with newly diagnosed multiple myeloma who cannot have autologous stem cell transplantation. Patients with multiple myeloma have limited treatment options and Darzalex, which works in a different way to existing treatments, represents 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/Find medicine/Human medicines/European public assessment reports.

This overview was last updated in 08-2018.