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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 medicine used in adults to treat the following conditions. .

Multiple myeloma

Darzalex is used to treat adults with multiple myeloma, a cancer of the bone marrow that affects a type of white blood cell called plasma cells, which normally help fight infections.

In patients with newly diagnosed multiple myeloma, Darzalex is used:

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

In patients with previously treated multiple myeloma, Darzalex is used:

- in combination with dexamethasone plus either lenalidomide or bortezomib;
- in combination with pomalidomide (another medicine to treat multiple myeloma) and dexamethasone when the disease has not improved with lenalidomide in combination with cancer medicines known as proteasome inhibitors, or when the disease has worsened after at least two treatments with these medicines;
- on its own when the disease has come back after treatment with cancer medicines (including proteasome inhibitors) and immunomodulatory medicines (that act on the immune system), or when the disease has not improved with these medicines.

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000
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Smouldering multiple myeloma

Darzalex is used on its own to treat adults with smouldering multiple myeloma, an early, pre-cancerous form of multiple myeloma with abnormal plasma cells in the bone marrow. It is used in patients whose disease has a high risk of progressing to multiple myeloma.

Light chain (AL) amyloidosis

Darzalex is used in patients newly diagnosed with AL amyloidosis, a blood disease in which deposits of abnormal proteins, called amyloids, accumulate and cause damage in tissues and organs. It is used in combination with cyclophosphamide, bortezomib and dexamethasone.

Multiple myeloma and AL amyloidosis are rare, and Darzalex was designated an 'orphan medicine' (a medicine used in rare diseases. Further information on the orphan designations can be found on the Agency's website (multiple myeloma: 17 July 2013, AL amyloidosis: 25 May 2018).

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. The first dose should be given in a place where resuscitation equipment is available in case of severe allergic reaction (anaphylaxis).

For multiple myeloma, smouldering multiple myeloma and AL amyloidosis, Darzalex is given by injection under the skin; for certain uses in multiple myeloma, it is given by infusion (drip) into a vein. How often Darzalex is given depends on the disease, which other medicines are being given and whether patients can have a transplant or not. 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 infusion-related reactions. If the patient has a severe reaction, 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 abnormal white blood cells in multiple myeloma and AL amyloidosis. By attaching to CD38 on these cells, daratumumab activates the immune system to kill the abnormal white blood 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 absence of, or at least a 50% reduction in, a protein produced by multiple myeloma cells). Around 29% of the patients receiving Darzalex at the recommended dose (31 out of 106 patients) responded to treatment in the first study and 36% (15 out of 42 patients) responded 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 got worse 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, which involved 569 patients, 78% of patients receiving Darzalex and dexamethasone plus lenalidomide lived for 18 months without their disease getting worse compared with 52% of those receiving dexamethasone plus lenalidomide. In the second study, which involved 498 patients, 61% of patients receiving Darzalex and dexamethasone plus bortezomib lived for 12 months without their disease getting worse compared with 27% of those receiving dexamethasone plus bortezomib.

Darzalex combined with pomalidomide and dexamethasone was investigated in 304 patients with multiple myeloma whose disease got worse after, or did not respond to, at least one previous treatment with lenalidomide and a proteasome inhibitor. In this study, patients receiving this combination lived for around 12 months without their disease getting worse, compared with 7 months for those receiving a combination of only pomalidomide and dexamethasone.

Another study, involving 522 patients with multiple myeloma that got worse or had not responded after previous treatment, showed that Darzalex given by injection under the skin was no less effective in treating the condition than Darzalex given by infusion into a vein; the disease responded in 41% (108 out of 263) of patients given the injection and 37% (96 out 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, which involved 737 patients, found that 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 a combination of bortezomib, melphalan and prednisone in a study involving 706 patients with newly diagnosed multiple myeloma who could not have an autologous stem cell transplant. After about 28 months, 70% (246 out of 350) of patients treated with Darzalex in combination with the other three medicines had no worsening of their disease compared with 49% (174 out of 356) of patients treated with the three other medicines.

Darzalex has also been studied in two studies involving patients who could have an autologous stem cell transplant. In the first 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.

The second study involved 709 adults who received either bortezomib, lenalidomide and dexamethasone combined with Darzalex or bortezomib, lenalidomide and dexamethasone without Darzalex, both given for 4 cycles before and 2 cycles after transplantation. Patients who received the combination with Darzalex continued to receive Darzalex with lenalidomide maintenance treatment, while those who received bortezomib, lenalidomide and dexamethasone without Darzalex received maintenance treatment with lenalidomide alone. Around 48 months after starting the study, 14% (50 out of 355) of patients who received the combination with Darzalex experienced worsening of their

disease compared with 29% (103 out of 354) of patients who received bortezomib, lenalidomide and dexamethasone without Darzalex.

In another study involving 395 people with untreated multiple myeloma for whom stem cell transplantation was not planned, treatment with Darzalex, bortezomib, lenalidomide and dexamethasone was compared with the same treatment without Darzalex. The main measure of effectiveness was the proportion of patients in whom minimal residual disease is no longer detectable in their body (so called minimal residual disease negativity). Minimal residual disease refers to the small number of cancer cells that might remain after treatment and could potentially cause a relapse. Minimal residual disease negativity was reached in 53% (105 out of 197) of patients receiving the treatment including Darzalex, compared with 35% (70 out of 198) of those not receiving Darzalex. In addition, at 39 months after the start of the study, 46 patients receiving Darzalex had a worsening of their disease or died, compared with 67 patients not receiving Darzalex.

AL amyloidosis

Darzalex in combination with cyclophosphamide, bortezomib and dexamethasone was compared with a combination of cyclophosphamide, bortezomib and dexamethasone without Darzalex in a study involving 388 patients with newly diagnosed AL amyloidosis. The main measure of effectiveness was the response to treatment based on a decrease in the levels of abnormal proteins in the blood. Around 53% of the patients that received the combination treatment with Darzalex had normal blood test results, compared with around 18% of the patients that used cyclophosphamide, bortezomib and dexamethasone.

Smouldering multiple myeloma

In a study involving 390 patients with smouldering multiple myeloma at high risk of progressing to multiple myeloma, treatment with Darzalex on its own was compared to active monitoring (where no treatment is given, but patients are closely followed for disease progression).

After patients had been in the study for an average of 65 months, those under active monitoring lived for an average of 41.5 months without their disease getting worse. This time could not be calculated in patients who received Darzalex due to the low number of patients whose disease worsened at the time of analysis.

Additionally, the study showed that the extent of the disease decreased in 63.4% of people taking Darzalex, compared with 2% in people being actively monitored.

What are the risks associated with Darzalex?

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

The most common side effects with Darzalex (which may affect more than 1 in 5 patients) include reactions to the infusion or injection, tiredness, weakness, COVID-19, fever, muscle and bone pain, 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 neuropathy (damage to the nerves in the arms and legs).

Some side effects can be serious. The most frequent with Darzalex include 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, atrial fibrillation (irregular rapid contractions of the upper chambers of the heart) and syncope (fainting).

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.

For multiple myeloma, Darzalex on its own or combined with other medicines is effective at treating patients whose disease had progressed despite previous treatment. Darzalex combined with other medicines is also effective at treating patients with newly diagnosed multiple myeloma who can or cannot have an autologous stem cell transplant.

In patients with newly diagnosed AL amyloidosis, adding Darzalex to cyclophosphamide, bortezomib and dexamethasone increased the effectiveness of this standard treatment.

At the time of approval, patients with multiple myeloma and AL amyloidosis had limited treatment options; Darzalex, which worked in a different way to existing treatments, represented a treatment alternative.

Darzalex was shown to prolong the time patients with smouldering multiple myeloma at high risk of progressing to multiple myeloma live without their disease getting worse. At the time of approval, Darzalex was the first medicine authorised for the treatment of smouldering multiple myeloma.

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 standard approval.

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

The company will provide educational material to all healthcare professionals expected to use the medicine, to inform them that the medicine can affect the results of a blood test (indirect Coombs test) used to determine suitability for blood transfusions. Patients prescribed Darzalex will receive 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 standard 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.

This overview was last updated in 07-2025.