EMA/426068/2023
EMEA/H/C/002455

Adcetris (*brentuximab vedotin*)

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

What is Adcetris and what is it used for?

Adcetris is a cancer medicine used to treat adults with certain lymphomas (cancers of lymphocytes, white blood cells that are part of the immune system). It is used when the cancer cells have a protein called CD30 on their surface (CD30-positive).

For Hodgkin's lymphoma (HL), it is given:

- together with doxorubicin, vinblastine and dacarbazine (other cancer medicines) in patients whose cancer is advanced (stage III or IV disease) and has not been treated before;
- when the cancer has come back or has not responded to an autologous stem cell transplant (a transplant of the patient's own blood-producing cells);
- if the cancer is likely to come back or get worse after an autologous stem cell transplant;
- when the cancer has come back or has not responded to at least two other therapies and when autologous stem cell transplant or multi-agent chemotherapy (a combination of cancer medicines) cannot be used;

In non-Hodgkin's lymphoma, Adcetris is used for:

- systemic anaplastic large cell lymphoma (sALCL, a cancer of lymphocytes called T-cells) when the cancer has never been treated before; Adcetris is used together with cyclophosphamide, doxorubicin and prednisone. It is also used when the cancer has come back or when other treatments have not worked;
- cutaneous T-cell lymphoma (CTCL), a lymphoma of T-cells that initially affects the skin, in patients who have received at least one previous treatment.

These diseases are rare, and Adcetris was designated an 'orphan medicine' (a medicine used in rare diseases). Further information on the orphan designations can be found on the European Medicines Agency's website (Hodgkin's lymphoma: 15 January 2009; cutaneous T-cell lymphoma: 11 January 2012; peripheral T-cell lymphoma: 21 August 2019).

Adcetris contains the active substance brentuximab vedotin.

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How is Adcetris used?

Adcetris can only be obtained with a prescription, and it should be given under the supervision of a doctor who has experience in the use of cancer treatments.

The recommended dose depends on body weight and whether Adcetris is given with other cancer medicines. The medicine is given by a 30-minute infusion (drip) into a vein every 2 or 3 weeks. When given with other cancer medicines, patients may also be given a medicine to help prevent neutropenia (low white blood cell count). Patients should be monitored during and after the infusion for certain side effects and they should have full blood counts (tests of the number of blood cells) before every dose of Adcetris.

The doctor may interrupt or stop treatment or reduce the dose if the patient develops certain serious side effects. For more information about using Adcetris, see the package leaflet or contact your doctor or pharmacist.

How does Adcetris work?

The active substance in Adcetris, brentuximab vedotin, is made up of a monoclonal antibody (a type of protein) that binds to CD30, linked to monomethyl auristatin E, a cytotoxic (cell-killing) molecule. The monoclonal antibody delivers monomethyl auristatin E to the CD30-positive cancer cells. The cytotoxic molecule then enters the cancer cells and stops them from dividing, and the cancer cells eventually die.

What benefits of Adcetris have been shown in studies?

Hodgkin's lymphoma

In a main study of 1,334 patients with CD30-positive HL who had not received previous treatment, Adcetris plus doxorubicin, vinblastine and dacarbazine was compared with bleomycin also given with doxorubicin, vinblastine and dacarbazine. After 2 years, 82% of patients given Adcetris lived without their disease getting worse, compared with 77% of patients given bleomycin. Patients also had a higher chance of surviving for 4 years with Adcetris (95%) than with bleomycin (92%).

In another main study, Adcetris was used in 102 patients with CD30-positive HL, who had previously received an autologous stem cell transplant and whose cancer had come back or had not responded to previous treatment. Response to treatment was assessed using body scans and patients' clinical data. A complete response is when a patient has no signs of cancer. In this study, the cancer responded partially or completely to treatment in 75% of patients (76 out of 102). A complete response occurred in 33% of patients (34 out of 102).

In addition, the company provided data on 40 patients with CD30-positive HL, whose cancer had come back or had not responded to at least 2 prior therapies and who were not eligible for autologous stem cell transplant or multi-agent chemotherapy. The cancer responded to treatment in 55% of patients (22 out of 40). For 23% of these patients (9 out of 40) a complete response was observed.

In another main study, Adcetris was compared with placebo (a dummy treatment) in 329 patients with CD30-positive HL who had received an autologous stem cell transplant and who were at increased risk of their cancer progressing or coming back. The average time patients lived before their disease got worse was around 43 months in those given Adcetris, compared with around 24 months in those receiving placebo. The benefit was sustained during 3 years of follow up.

Systemic anaplastic large cell lymphoma

Adcetris was studied in 452 patients with CD30+ peripheral T cell lymphoma (PTCL) of whom about 70% had sALCL. The patients had not been treated for their cancer before and received either Adcetris plus cyclophosphamide, doxorubicin and prednisone, or cyclophosphamide, doxorubicin, vincristine and prednisone. Patients with sALCL who were treated with Adcetris lived on average 56 months without their disease progressing compared with 54 months in the other group. In addition, after 2 years, 68% of patients given Adcetris lived without their disease getting worse, compared with 54% of patients in the other group. Since most patients in the study had sALCL and many other types of PTCL with different prognoses were not represented, it was considered that the effectiveness of Adcetris in the broader PTCL indication was not demonstrated.

Adcetris was also studied in 58 sALCL patients whose cancer had come back or had not responded to treatment. In this study, 86% of patients (50 out of 58) responded partially or completely to treatment and response was complete for 59% (34 out of 58). Results from an additional study involving 50 sALCL patients confirmed the benefits of Adcetris in this patient population.

Cutaneous T-cell lymphoma

Adcetris was effective in CD30-positive cutaneous T-cell lymphoma in a main study involving 128 patients with CD30-positive CTCL who had had at least one previous treatment. The study compared treatment with Adcetris and treatment with another medicine (methotrexate or bexarotene). The proportion of patients whose disease responded to treatment for at least 4 months was 56% of those given Adcetris (36 of 64 patients) and 13% of those given alternative treatments (8 of 64 patients).

What are the risks associated with Adcetris?

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

The most common side effects of Adcetris (which may affect more than 1 in 10 people) include infections (including infections of the nose and throat), peripheral sensory or motor neuropathy (nerve damage that affects feeling or muscle control and coordination), tiredness, nausea (feeling sick), diarrhoea, fever, neutropenia (low levels of a type of white blood cell), rash, cough, vomiting, joint pain, infusion-related reactions, itching, constipation, dyspnoea (difficulty breathing), weight loss, muscle pain and abdominal (belly) pain.

Adcetris must not be used together with bleomycin (another cancer medicine) as this combination is damaging to the lungs.

Why is Adcetris authorised in the EU?

The European Medicines Agency noted that, despite limited data and paucity of studies that compared Adcetris with a control treatment, Adcetris was considered beneficial for patients with HL and sALCL whose cancer had come back or had not responded to therapy. In these patients, who generally have poor outcomes and lack suitable treatments, Adcetris could lead to a cure or could enable them to undergo potentially curative treatments. In addition, giving Adcetris to patients who have had a stem cell transplant and are considered at risk of the cancer progressing or coming back, resulted in a clear clinical benefit. Previously untreated patients with advanced HL or with sALCL also benefited from Adcetris used in combination with other cancer medicines. In patients with CTCL, a clinically significant benefit was seen over treatment with bexarotene or methotrexate. The Agency further noted that the overall safety profile of Adcetris was acceptable given the serious conditions for which it is used.

Therefore, the Agency decided that the benefits of Adcetris are greater than its risks and it can be authorised for use in the EU.

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

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

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

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

Other information about Adcetris

Adcetris received a conditional marketing authorisation valid throughout the EU on 25 October 2012. This was switched to a full marketing authorisation on 24 May 2022.

Further information on Adcetris can be found on the Agency's website: ema.europa.eu/medicines/human/EPAR/adcetris.

This overview was last updated in 10-2023.