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EPAR summary for the public

Adcetris

brentuximab vedotin

This is a summary of the European public assessment report (EPAR) for Adcetris. It explains how the Agency assessed the medicine to recommend its authorisation in the EU and its conditions of use. It is not intended to provide practical advice on how to use Adcetris.

For practical information about using Adcetris, patients should read the package leaflet or contact their doctor or pharmacist.

What is Adcetris and what is it used for?

Adcetris is a cancer medicine used to treat adults with Hodgkin's lymphoma (HL, a type of cancer that originates from blood cells in the lymphatic system, a part of the immune system) when the tumour cells are CD30-positive (when they have a protein called CD30 on their surface). It is used:

- 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);
- when patients have had an autologous stem cell transplant but are considered to be at increased risk of the cancer coming back or not responding;
- 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.

Adcetris is also used to treat adults with systemic anaplastic large cell lymphoma (sALCL, a CD30-positive cancer of white blood cells called T lymphocytes), when the cancer has come back or has not responded to other treatments.

Because the number of patients with HL and sALCL is low, the diseases are considered 'rare', and Adcetris was designated an 'orphan medicine' (a medicine used in rare diseases) on 15 January 2009.

Adcetris contains the active substance brentuximab vedotin.



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 is 1.8 mg per kilogram body weight given by a 30-minute infusion (drip) into a vein every three weeks. Patients should be monitored during and after the infusion for certain side effects and they should have full blood counts checked before every dose of Adcetris. Treatment should continue for up to 1 year unless the disease gets worse or severe side effects develop.

The doctor may interrupt or stop treatment, or reduce the dose, if the patient develops certain serious side effects. For further information, see the package leaflet.

How does Adcetris work?

The active substance in Adcetris, brentuximab vedotin, is made up of a CD30 monoclonal antibody (a type of protein that attaches to CD30). The monoclonal antibody is attached to monomethyl auristatin E, a cytotoxic (cell-killing) molecule. The monoclonal antibody delivers monomethyl auristatin E to the CD30-positive cancer cells, and once inside the cancer cells, it 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, 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. The main measure of effectiveness was the percentage of patients who responded completely or partially to 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, 75% of patients (76 out of 102) responded partially or completely to treatment. A complete response was observed 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 two prior therapies and who were not eligible for autologous stem cell transplant or multi-agent chemotherapy. The data on these patients showed that 55% of patients (22 out of 40) responded to treatment. 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 main measure of effectiveness was how long patients lived without their disease getting worse. In this study, the average length of time patients lived before their disease got worse was around 43 months in those given Adcetris, compared with around 24 months in those given placebo. The benefit was sustained after 3 years of follow-up.

Systemic anaplastic large cell lymphoma

Adcetris was studied in 58 sALCL patients whose cancer had come back or had not responded to treatment. The main measure of effectiveness was the percentage of patients who responded completely or partially to 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, 86% of patients (50 out of 58) responded partially or completely to treatment and this response was complete for 59% of them (34 out of 58).

What are the risks associated with Adcetris?

Serious side effects reported with Adcetris include pneumonia (lung infection), acute respiratory distress syndrome (a condition where inflammation and fluid in the lungs lead to difficulty breathing), headache, neutropenia (low white blood cell counts), thrombocytopenia (low blood platelet counts), constipation, diarrhoea, vomiting, nausea (feeling sick), fever, peripheral motor neuropathy (damage to the nerves causing difficulty co-ordinating movements) and peripheral sensory neuropathy (nerve damage affecting sensation in the hands and feet), hyperglycaemia (high blood glucose levels), demyelinating polyneuropathy (a neurological disorder characterized by slowly progressive weakness and a loss of sensation in the legs and arms), tumour lysis syndrome (a potentially fatal complication due to the breakdown of cancer cells) and Stevens-Johnson syndrome (a life-threatening type of allergic reaction affecting the skin and mucous membranes). The most frequent side effects (which may affect more than 2 in 10 people) include peripheral sensory neuropathy, tiredness, nausea, diarrhoea, upper respiratory tract infections (nose and throat infection), neutropenia and cough.

Adcetris must not be used together with bleomycin (another cancer medicine) as this combination is damaging to the lungs. For the full list of all side effects and restrictions with Adcetris, see the package leaflet.

Why has Adcetris been approved?

The European Medicines Agency noted that, despite limited data and studies that did not compare 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. The Agency further noted that the overall safety profile of Adcetris was acceptable for these patients. Therefore, the Agency decided that Adcetris' benefits are greater than its risks and recommended that it be approved for use in the EU.

Adcetris has been given 'conditional approval'. This means that there is more evidence to come, especially about the medicine's long-term effects, which are needed to confirm the positive benefit-risk balance. Every year, the European Medicines Agency will review any new information that may become available and this summary will be updated as necessary.

What information is still awaited for Adcetris?

The company that markets the medicine will carry out a study on the benefits of the medicine in sALCL patients and a safety study in a larger population of HL and sALCL patients.

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.

Other information about Adcetris

The European Commission granted a conditional marketing authorisation valid throughout the European Union for Adcetris on 25 October 2012.

The full EPAR for Adcetris can be found on the Agency's website: ema.europa.eu/Find_medicine/Human_medicines/European_public_assessment_reports. For more information about treatment with Adcetris, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

The summary of the opinion of the Committee for Orphan Medicinal Products for Adcetris can be found on the Agency's website:

- [Hodgkin's lymphoma](#);
- [Anaplastic large cell lymphoma](#).

This summary was last updated in 08-2017.