Package leaflet: Information for the patient

Adcetris 50 mg powder for concentrate for solution for infusion
brentuximab vedotin

▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects.

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Adcetris is and what it is used for
2. What you need to know before you are given Adcetris
3. How Adcetris will be given
4. Possible side effects
5. How to store Adcetris
6. Contents of the pack and other information

1. What Adcetris is and what it is used for

Adcetris contains the active substance **brentuximab vedotin**, an anti-cancer agent, which is made up of a monoclonal antibody linked to a substance intended to kill cancer cells. This substance is delivered to cancer cells by the monoclonal antibody. A monoclonal antibody is a protein which recognises certain cancer cells.

Adcetris is used to treat classical Hodgkin lymphoma that has:
- come back after or not responded to an infusion of your own healthy stem cells into your body (autologous stem cell transplant), or
- come back after or never responded to at least two previous therapies, and where you cannot receive additional combination anti-cancer treatments or have an autologous stem cell transplant.

Classical Hodgkin lymphoma expresses specific proteins on the cell surface that are different from non-classical Hodgkin lymphoma.

Adcetris is used to treat systemic anaplastic large cell lymphoma which is found in your lymph nodes and/or throughout other parts of your body that has:
- not responded to other types of anti-cancer treatments, or
- come back after previous anti-cancer treatment.

Hodgkin lymphoma and systemic anaplastic large cell lymphoma are both types of cancer of the white blood cells.

2. What you need to know before you are given Adcetris

Do NOT use Adcetris if you:

- are allergic to brentuximab vedotin or any of the other ingredients of this medicine (listed in section 6).

- are currently using bleomycin, an anti-cancer agent

Warnings and precautions

When you first receive this medicine and during the course of treatment, tell your doctor if you:
- have confusion, trouble thinking, memory loss, blurred or loss of vision, decreased strength, decreased control or sensation in one arm or leg, a change in the way of walking, or loss of balance, as these may be symptoms of a serious and potentially fatal brain condition known as progressive multifocal leukoencephalopathy (PML). If you have these symptoms prior to treatment with this medicine, tell your doctor immediately about any changes in these symptoms. You should also inform your partner or caregivers about your treatment, since they may notice symptoms that you are not aware of.
- have severe and persistent stomach pain, with or without nausea and vomiting, as these may be symptoms of a serious and potentially fatal condition known as pancreatitis (inflammation of the pancreas).
- have new or worsening shortness of breath or cough
- are taking, or have previously taken, medicines which may affect your immune system, such as chemotherapy or immunosuppressive agents
- have, or think you have, an infection. Some infections may be serious and can be due to viruses, bacteria, or other causes that may be life-threatening
- experience a whistling sound during breathing (wheezing)/difficulty breathing, hives, itching, or swelling (signs of an infusion reaction). For more detailed information, see "Infusion reactions" in section 4.
- have any problems with a change in the sensitivity of the skin, especially in the hands or feet, such as numbness, tingling, a burning sensation, pain, discomfort or weakness (neuropathy)
- have headaches, feel tired, experience dizziness, look pale (anaemia), or have unusual bleeding or bruising under the skin, longer than usual bleeding after your blood has been drawn, or bleeding from your gums (thrombocytopenia)
- develop chills or shivering, or feel warm; you should take your temperature as you may have a fever. A fever with a low white blood cell count may be a sign of serious infection
- experience dizziness, decreased urination, confusion, vomiting, nausea, swelling, shortness of breath, or heart rhythm disturbances (this may be a potentially life-threatening complication known as tumour lysis syndrome)
- experience flu-like symptoms followed by a painful red or purplish rash that spreads and blisters including extensive detachment of the skin that may be life-threatening (this may be a serious skin reaction known as Stevens-Johnson syndrome and toxic epidermal necrolysis)
- feel tired, have frequent urination, increased thirst, increased appetite with unintended weight loss, or irritability (hyperglycaemia)
- have kidney or liver problems.

Your doctor will perform regular blood tests to make sure that it is safe for you to receive this medicine.

Other medicines and Adcetris

Tell your doctor if you are taking any other medicines, if you have taken any recently, or if you start taking new ones. This includes herbal medicines and other medicines you can obtain without a prescription.

Pregnancy, breast-feeding and fertility

You and your partner must use two methods of effective contraception during your treatment with this medicine. Women must continue using contraception for 6 months following the last dose of Adcetris.

You should not use this medicine if you are pregnant unless you and your doctor decide that the benefit to you outweighs the potential risk to the unborn baby.

It is important to tell your doctor before and during treatment if you are pregnant, think you may be pregnant, or are planning to get pregnant.

If you are breast-feeding, you should discuss with your doctor whether you should receive this medicine.

Men being treated with this medicine are advised to have sperm samples frozen and stored before treatment. Men are advised not to father a child during treatment with this medicine and for up to 6 months following the last dose of this medicine.

Driving and using machines

Your treatment may influence your ability to drive or operate machines. If you feel unwell during treatment then do not drive or operate machines.

Adcetris contains sodium

This medicine contains a maximum of 2.1 mmol (or 47 mg) sodium per dose. To be taken into consideration by patients on a controlled sodium diet.

3. How Adcetris will be given

If you have any questions on the use of this medicine, ask the doctor or nurse who is giving you the infusion.

Dose and frequency

The dose of this medicine depends on your body weight. The usual starting dose of Adcetris is 1.8 mg/kg, given once every 3 weeks for no more than one year. Your doctor may lower your starting dose to 1.2 mg/kg if you have kidney or liver problems.

Adcetris is to be given to adults only. It is not for use in children.

How Adcetris is given

This medicine is given to you into a vein (intravenously) as an infusion. It is given by your doctor or nurse over 30 minutes. Your doctor or nurse will also monitor you during and after the infusion.

If you have any other questions on the use of this medicine, ask your doctor.

4. Possible side effects

Like all medicines, this medicine may cause side effects, although not everybody gets them.

Infusion reactions

Medicines of this type (monoclonal antibodies) can cause infusion reactions such as:
- a rash
- shortness of breath
- difficulty breathing
- a tight chest
- fever
- back pain.

Infusion reactions to this medicine affect more than 1 in 10 people.

In general, these types of reactions occur within minutes to several hours following completion of the infusion. However, they may develop more than several hours after completion of the infusion but this is uncommon. These infusion reactions can be serious or even fatal (known as an anaphylactic reaction). It is not known how frequently infusion-related reactions to this medicine are serious or fatal.

You may be given other medicines such as
- anti-histamines, corticosteroids or paracetamol

to help reduce any of the reactions above if you have already experienced these when receiving this type of medicine.

If you think you have previously had a similar reaction, tell your doctor BEFORE you are given this medicine.
If you develop infusion reactions (as stated previously), your doctor may stop giving this medicine and start support treatment.
If your infusion is restarted, your doctor may increase the time over which your infusion is given so that you may be able to tolerate it better.

Tell your doctor straight away if you notice any of the following symptoms because some of them may be signs of a serious or possibly fatal condition:
- Progressive multifocal leukoencephalopathy (PML) symptoms such as confusion, trouble thinking, memory loss, blurred or loss of vision, decreased strength, decreased control or sensation in one arm or leg, a change in the way of walking, or loss of balance (for more detailed information, see section 2). The frequency of this condition cannot be estimated from the available data.
- Symptoms of inflammation of the pancreas (pancreatitis) such as severe and persistent stomach pain, with or without nausea and vomiting (affects less than 1 in 100 people).
- flu-like symptoms followed by a painful red or purplish rash that spreads and blisters including extensive detachment of the skin (affects less than 1 in 1000 people)
- a change in feeling or sensitivity, especially in the skin, numbness, tingling, discomfort, a burning sensation, weakness, or pain in the hands or feet (neuropathy; affects more than 1 in 10 people)
- a feeling of weakness (affects more than 1 in 10 people)
- constipation (affects less than 1 in 10 people)
- diarrhoea, vomiting (affects more than 1 in 10 people)
- chills or shivering (affects less than 1 in 10 people)
- feeling tired, frequent urination, increased thirst, increased appetite with unintended weight loss, and irritability (these may be signs of hyperglycaemia, which affects less than 1 in 10 people)
- unusual bleeding or bruising under the skin, longer than usual bleeding after your blood has been drawn, or bleeding from your gums (these may be signs of thrombocytopenia which affects less than 1 in 10 people)
- headaches, experience dizziness, look pale (these may be signs of anaemia, which affects less than 1 in 10 people)

You may experience the following side effects:

Very common side effects (affects more than 1 in 10 people)
- decreased level of white blood cells
- infection
- nausea
- itching
- unusual hair loss or thinning
- muscle pain

Common side effects (affects less than 1 in 10 people)
- an infection in the blood (sepsis) and/or septic shock (a life-threatening form of sepsis);cough; upper respiratory tract infection; pneumonia
- decreased level of blood platelets
- dizziness
- joint pain or painful, swollen joints
- blisters which may crust or scab
- increased level of blood sugar
- increased liver enzyme levels

Uncommon side effects (affects less than 1 in 100 people)
- Tumour lysis syndrome – a potentially-life threatening condition in which you may experience dizziness, decreased urination, confusion, vomiting, nausea, swelling, shortness of breath, or heart rhythm disturbances.
- sore, creamy-yellow, raised patches in the mouth (thrush)

Rare side effects (affects less than 1 in 1000 people)
- Stevens-Johnson syndrome and toxic epidermal necrolysis - a rare, serious disorder in which you may experience flu-like symptoms followed by a painful red or purplish rash that spreads and blisters including extensive detachment of the skin

Not known (frequency cannot be estimated from the available data)
- decreased level of white blood cells with a fever

Reporting of side effects

If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Adcetris

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the vial label and the carton after EXP. The expiry date refers to the last day of that month.

Unopened vial: Store in a refrigerator (2°C-8°C). Do not freeze.
Keep the vial in the original carton in order to protect from light.

Reconstituted/diluted solution: Use immediately or store in a refrigerator (2°C-8°C) and use within 24 hours.

Do not use this medicine if you notice any particulate matter or discoloration prior to administration.

Do not throw away any medicines via wastewater or household waste. The doctor or nurse will dispose of this medicine. These measures will help protect the environment.

6. Contents of the pack and other information

What Adcetris contains

- The active substance is brentuximab vedotin. Each vial contains 50 mg of brentuximab vedotin. After reconstitution each ml of solution contains 5 mg of Adcetris.

- The other ingredients are citric acid monohydrate, sodium citrate dihydrate, α,α-trehalose dihydrate, and polysorbate 80. See section 2 for further information about sodium.

What Adcetris looks like and contents of the pack

Adcetris is a white to off-white cake or powder for concentrate for solution for infusion provided in a glass vial.

Each pack of Adcetris consists of one vial.

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This medicine has been given ‘conditional approval’. This means that there is more evidence to come about this medicine.
The European Medicines Agency will review new information on this medicine at least every year and this leaflet will be updated as necessary.

Detailed information on this medicine is available on the European Medicines Agency website: http://www.ema.europa.eu/

The following information is intended for healthcare professionals only:

Instructions for reconstitution

Each single use vial must be reconstituted with 10.5 ml of water for injections to a final concentration of 5 mg/ml. Each vial contains a 10% overfill giving 55 mg of ADCETRIS per vial and a total reconstituted volume of 11 mL.

1. Direct the stream toward the wall of the vial and not directly at the cake or powder.
2. Gently swirl the vial to aid dissolution. DO NOT SHAKE.
3. The reconstituted solution in the vial is a clear to slightly opalescent, colourless solution with a final pH of 6.6.
4. The reconstituted solution should be inspected visually for any foreign particulate matter and/or discoloration. In the event of either being observed, discard the medicinal product.

Preparation of Infusion Solution

The appropriate amount of reconstituted Adcetris must be withdrawn from the vial(s) and added to an infusion bag containing sodium chloride 9 mg/ml (0.9%) solution for injection in order to achieve a final concentration of 0.4-1.2 mg/ml Adcetris. The recommended diluent volume is 150 ml. The already reconstituted Adcetris can also be diluted into 5% dextrose for injection or Lactated Ringer's for injection.

Gently invert the bag to mix the solution containing Adcetris. DO NOT SHAKE.

Any portion left in the vial, after withdrawal of the volume to be diluted, must be disposed of in accordance with local requirements.

Do not add other medicinal products to the prepared Adcetris infusion solution or intravenous infusion set. The infusion line should be flushed following administration with sodium chloride 9 mg/ml (0.9%) solution for injection, 5% dextrose for injection, or Lactated Ringer's for injection.

Following dilution, infuse the Adcetris solution immediately at the recommended infusion rate.

Total storage time of the solution from reconstitution to infusion should not exceed 24 hours.

Disposal

Adcetris is for single use only.

Any unused product or waste material should be disposed of in accordance with local requirements.