Package leaflet: Information for the patient

Adakveo 10 mg/ml concentrate for solution for infusion
crizanlizumab

▼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 are given 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 or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Adakveo is and what it is used for

What Adakveo is
Adakveo contains the active substance crizanlizumab, which belongs to a group of medicines called monoclonal antibodies (mAbs).

What Adakveo is used for
Adakveo is used to prevent recurrent painful crises occurring in patients aged 16 years and over with sickle cell disease. Adakveo can be given in combination with hydroxyurea/hydroxycarbamide, although it may also be used alone.

Sickle cell disease is an inherited blood disorder. It causes affected red blood cells to become sickle-shaped and have difficulty passing through small blood vessels. Additionally in sickle cell disease the blood vessels are damaged and sticky due to ongoing chronic inflammation. This leads to blood cells sticking to the blood vessels, causing acute episodes of pain and organ damage.

How Adakveo works
Patients with sickle cell disease have higher levels of a protein called P-selectin. Adakveo binds P-selectin. This should stop blood cells sticking to the vessel walls and help prevent painful crises.

If you have any questions about how Adakveo works or why this medicine has been prescribed for you, ask your doctor or nurse.

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

You must not be given Adakveo:
- if you are allergic to crizanlizumab or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions

Infusion-related reactions
Medicines of this type (called monoclonal antibodies) are administered into a vein (intravenously) as an infusion. They can cause unwanted reactions (side effects) when they are infused into your body. Such reactions may happen during infusion or within 24 hours of receiving an infusion.

Tell your doctor or nurse immediately if you experience any of the following symptoms during infusion or within 24 hours of the infusion, as these may be signs of an infusion-related reaction:
- Pain in various locations, headache, fever, chills or shivering, nausea, vomiting, diarrhoea, tiredness, dizziness, itching, hives, sweating, shortness of breath or wheezing. See also section 4, "Possible side effects".

Your doctor or nurse may monitor you for signs and symptoms of such infusion-related reactions.

If you experience an infusion-related reaction, the Adakveo infusion may need to be stopped or slowed down. You may be given additional medicines to treat the symptoms of infusion-related reaction. Your next Adakveo infusions may continue to be given more slowly and/or with medicines to reduce the risk of an infusion-related reaction.

Blood tests during Adakveo treatment
If you need to have any blood tests, tell the doctor or nurse that you are on treatment with Adakveo. This is important because this treatment may interfere with a laboratory test used to measure the number of platelets in your blood.

Children and adolescents
Adakveo should not be used in children or adolescents below 16 years of age.

Other medicines and Adakveo
Tell your doctor or nurse if you are taking, have recently taken or might take any other medicines.

Pregnancy and breast-feeding
Adakveo has not been tested in pregnant women therefore there is limited information about its safety in pregnant women.

If you are pregnant, or are a woman who could become pregnant and is not using contraception, it is not recommended to use Adakveo.

It is not known whether Adakveo or its individual ingredients pass into breast milk.

If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor for advice before receiving this medicine. Your doctor will discuss with you the potential risk(s) of Adakveo during pregnancy or breast-feeding.

Driving and using machines
Adakveo could have a minor effect on your ability to drive and use machines. If you experience tiredness, drowsiness or dizziness, do not drive or use machines until you feel better.

Adakveo contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially "sodium-free".

3. How Adakveo is given

Adakveo will be given to you by a doctor or nurse.

If you have any questions about how Adakveo is given, ask the doctor or nurse who is giving you the infusion.

Your doctor will tell you when you will have your infusions and follow-up appointments.

How much Adakveo you will be given
The recommended dose is 5 mg per kilogram of body weight. You will be given the first infusion at Week 0 and the second infusion two weeks later (Week 2). After that you will be given an infusion every 4 weeks.

How the infusion is given
Adakveo is administered into a vein (intravenously) as an infusion lasting 30 minutes.

Adakveo can be given alone or with hydroxyurea/hydroxycarbamide.

How long Adakveo treatment lasts
You should discuss with your doctor how long you will need to receive treatment. Your doctor will regularly monitor your condition to check that the treatment is having the desired effect.

If you forget a Adakveo infusion
It is very important that you receive all your infusions. If you miss an appointment for an infusion, contact your doctor as soon as possible to reschedule.

If you stop Adakveo treatment
Do not stop Adakveo treatment unless your doctor tells you that you can.

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

4. Possible side effects

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

Some side effects could be serious
Tell the doctor or nurse giving you the infusion immediately if you develop any of the following symptoms during infusion or within 24 hours of the infusion:
- pain in various locations, headache, fever, chills or shivering, nausea, vomiting, diarrhoea, tiredness, dizziness, itching, hives, sweating, shortness of breath or wheezing.

These symptoms can be signs of infusion-related reaction, which is a common side effect (this means it may affect up to 1 in every 10 people).

Other possible side effects
Other possible side effects include those listed below. If these side effects become severe, tell your doctor or nurse.

Very common (may affect more than 1 in 10 people)
- pain in the joints (arthralgia)
- nausea
- back pain
- fever
- pain in the lower or upper abdomen, feeling of tenderness in the abdomen and abdominal discomfort

Common (may affect up to 1 in every 10 people)
- diarrhoea
- itching (including vulvovaginal itching)
- vomiting
- muscle pain (myalgia)
- pain in the muscles or bones of the chest (musculoskeletal chest pain)
- sore throat (oropharyngeal pain)
- redness or swelling and pain at the site of the infusion

Not known (frequency cannot be estimated from the available data)
- pain of any intensity (mild, moderate or severe) occuring in various locations during infusion or within 24 hours of the infusion, which may be a sign of an infusion-related reaction

Reporting of side effects
If you get any side effects, talk to your doctor or nurse. 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 or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Adakveo

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 outer carton and the label after "EXP". The expiry date refers to the last day of that month.

Keep the vial in the outer carton in order to protect from light. Store in a refrigerator (2°C – 8°C). Do not freeze.

Infusion solutions should be used immediately after dilution.

6. Contents of the pack and other information

What Adakveo contains
- The active substance is crizanlizumab. Each 10 ml vial contains 100 mg of crizanlizumab.
- The other ingredients are sucrose, sodium citrate (E331), citric acid (E330), polysorbate 80 (E433) and water for injections.

What Adakveo looks like and contents of the pack
Adakveo concentrate for solution for infusion is a colourless to slightly brownish-yellow liquid.

Adakveo is available in packs containing 1 vial.

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This leaflet was last revised in 03/2022.

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

The following information is intended for healthcare professionals only:

Adakveo vials are for single use only.

Preparing the infusion

The diluted solution for infusion should be prepared by a healthcare professional using aseptic techniques.

The total dose and required volume of Adakveo depend on the patient's body weight; 5 mg of crizanlizumab is administered per kg body weight.

The volume to be used for the preparation of the infusion is calculated according to the following equation:

$$\text{Volume (ml)} = \frac{\text{Patient's body weight (kg) x prescribed dose [5 mg/kg]}}{\text{Concentration of Adakveo [10 mg/ml]}}$$

1. Obtain the number of vials required to deliver the prescribed dose and bring them to room temperature (for a maximum of 4 hours). One vial is needed for every 10 ml of Adakveo (see below table).

Body weight (kg)	**Dose (mg)**	**Volume (ml)**	**Vials (n)**
40	200	20	2
60	300	30	3
80	400	40	4
100	500	50	5
120	600	60	6

2. Visually inspect the vials.
   - The solution in the vials should be clear to opalescent. Do not use if particles are present in the solution.
   - The solution should be colourless or may have a slight brownish-yellow tint.

3. Withdraw a volume equal to the required volume of Adakveo from a 100 ml infusion bag containing either sodium chloride 9 mg/ml (0.9%) solution for injection or dextrose 5% and discard.
   - No incompatibilities between the diluted Adakveo solution and infusion bags composed of polyvinylchloride (PVC), polyethylene (PE) and polypropylene (PP) have been observed.

4. Withdraw the necessary volume of Adakveo from the vials and inject slowly into the previously prepared infusion bag.
   - The solution must not be mixed or co-administered with other medicinal products through the same intravenous line.
   - Keep the volume of Adakveo added to the infusion bag in the range of 10 ml to 96 ml to obtain a final concentration in the infusion bag within 1 mg/ml to 9.6 mg/ml.

5. Mix the diluted solution by gently inverting the infusion bag. DO NOT SHAKE.

Storage of the diluted solution

Chemical and physical in-use stability, from the start of preparation of the diluted solution for infusion until end of infusion, has been demonstrated for up to 8 hours at room temperature (up to 25°C) and at 2°C to 8°C for up to 24 hours overall.

From a microbiological point of view, the diluted solution for infusion should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2°C to 8°C, including 4.5 hours at room temperature (up to 25°C) from the start of preparation to completion of the infusion, unless dilution has taken place in controlled and validated aseptic conditions.

Administration

Adakveo diluted solution must be administered through a sterile, non-pyrogenic 0.2 micron in-line filter by intravenous infusion over a period of 30 minutes. No incompatibilities have been observed between Adakveo and infusion sets composed of PVC, PE-lined PVC, polyurethane, and in-line filter membranes composed of polyethersulfone (PES), polyamide (PA) or polysulphone (PSU).

After administration of Adakveo, flush the line with at least 25 ml sodium chloride 9 mg/ml (0.9%) solution for injection or dextrose 5%.

Disposal

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