PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986
The medicine is dispensed with a doctor's prescription only

ADAKVEO® 10 mg/ml

Concentrate for solution for infusion

Active ingredient
Each 1 ml contains 10 mg crizanlizumab.
Each vial contains 10 ml.
Inactive and allergenic ingredients: see section 2 "Important information about some of the ingredients in the medicine" and section 6 "Further information".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Adakveo is indicated to reduce the frequency of vasoocclusive crises (VOCs) in adults and pediatric patients aged 16 years and older with sickle cell disease.

Therapeutic group: Monoclonal antibodies (mAbs)

2. BEFORE USING THE MEDICINE

Do not use this medicine if:

- you are sensitive (allergic) to the active ingredient crizanlizumab or to any of the additional ingredients contained in the medicine (see section 6).

Special warnings regarding use of this medicine
Before treatment with Adakveo, tell the doctor about your medical condition, including if you are pregnant or breastfeeding.

Adakveo may cause serious side effects, including:

- **Infusion-related reactions. Infusion-related reactions may occur during or within 24 hours of receiving an infusion of Adakveo. Infusion-related reactions may cause pain in different areas of your body.**
- The doctor may slow down, temporarily stop, or completely stop the Adakveo infusion if you have an infusion-related reaction. You may continue to receive Adakveo at a slower infusion rate and the doctor may give you certain medicines before the infusion to lower the risk of getting an infusion-related reaction. The doctor should monitor you for signs and symptoms of infusion-related reactions and treat the symptoms as needed.
- **Tell the doctor immediately if you develop any of the signs or symptoms of an infusion-related reaction listed below:**
  - pain in different areas of your body
  - headache
  - fever
  - chills or shivering
  - nausea
  - vomiting
  - diarrhea
  - tiredness
  - dizziness
  - sweating
  - hives
  - itching
  - shortness of breath or wheezing
- **Adakveo may interfere with a certain blood test.** Before performing any blood tests, tell the doctors treating you that you are receiving Adakveo. Adakveo may interfere with a laboratory test used to measure platelet count. For further information on possible side effects, see Section 4 "Side effects".

Children and adolescents
Adakveo is not indicated for use in children or adolescents under 16 years of age.
There is no information regarding the safety and efficacy of Adakveo in children and adolescents under the age of 16.

Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines or nutritional supplements, tell the doctor or pharmacist.

Pregnancy and breastfeeding

Pregnancy
Tell the doctor if you are pregnant or are planing to become pregnant. Adakveo may harm the unborn baby. Talk to your doctor about the possible risk to your unborn baby if you take Adakveo during pregnancy.

Breastfeeding
Tell the doctor if you are breastfeeding or are planing to breastfeed. It is not known if Adakveo passes into breast milk. You and the doctor will have to make a decision about the best way to feed your baby during the course of treatment with Adakveo.

Driving and operating machinery
Adakveo may have a minor influence on the ability to drive and use machines. Dizziness and fatigue may occur following administration of crizanlizumab.

Important information about some of the ingredients in the medicine
Adakveo contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per vial, i.e., it is considered to be essentially "sodium-free".

3. HOW SHOULD YOU USE THE MEDICINE?

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation. The dosage and treatment regimen will be determined by the doctor only.

- Adakveo is given as an infusion into the vein (intravenous administration) over 30 minutes. Adakveo will be given to you by a doctor or nurse.
- You will receive the first infusion, and then a second infusion 2 weeks later. After that, you will receive an infusion every 4 weeks.
- The doctor may also prescribe other medicines for you to take during the course of treatment with Adakveo.
- If you missed an infusion appointment, call the doctor as soon as possible to schedule a new appointment.

Adhere to the treatment regimen recommended by the doctor.
Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

If you have further questions regarding use of this medicine, consult a doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Adakveo may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Adakveo may cause serious side effects associated with infusion-related reaction. Tell the doctor immediately if you develop any of the following signs or symptoms of an infusion-related reaction (see section 2 "Special warnings regarding use of this medicine"):

- pain in different areas of your body
- headache
- fever
- chills or shivering
- nausea
- vomiting
- diarrhea
- tiredness
- dizziness
- sweating
- hives
- itching
- shortness of breath or wheezing

The most common side effects of Adakveo include:

- headache
- joint pains
- nausea
- back pain
- fatigue
- stomach pain
- fever
- diarrhea
- vomiting
- sore throat (oropharyngeal pain)

Additional side effects include:

- itch (including vaginal itch)
- pain in the muscles or bones of the chest (musculoskeletal pain in the chest)
- muscle pain (myalgia)
- infusion site redness or swelling and pain
- dizziness

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult with the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Reporting side effects following drug treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the following link: https://sideeffects.health.gov.il

Side effects can also be reported to Novartis company via the email address: safetydesk.israel@novartis.com

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine, and any other medicine, should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (exp. date) appearing on the package/vial. The expiry date refers to the last day of that month.

Storage conditions:
Store in a refrigerator (2°C – 8°C) in the original package to protect from light. Do not freeze.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Sucrose, sodium citrate, citric acid, polysorbate 80 and water for injection.

What the medicine looks like and the contents of the package:
A colorless to slightly brownish-yellow liquid in a 10 ml vial.
Each package contains 1 vial.

Registration holder and Importer and its address: Novartis Israel Ltd., P.O.B. 7126, Tel Aviv.

Revised in July 2024.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 168-71-36562

הוראות שימוש לצוות הרפואי

INSTRUCTIONS FOR USE FOR HEALTHCARE PROFESSIONALS

تعليمات الإستعمال للطاقم الطبي

Preparation and Administration

ADAKVEO should be prepared and administered by a healthcare professional.

Preparation

- Use aseptic technique to prepare the solution for infusion.
- Calculate the dose (mg) and the total volume (mL) of ADAKVEO solution required, and the number of ADAKVEO vials needed based on the patient's actual body weight.
  - Prepare 5 mg of ADAKVEO per kg of actual body weight.
- Calculate the volume of ADAKVEO to be used according to the following equation:

$$\text{Volume (mL)} = \frac{\text{patient's body weight (kg) x prescribed dose } \left[\frac{5\text{ mg}}{\text{kg}}\right]}{\text{concentration of ADAKVEO } \left[\frac{10\text{ mg}}{\text{mL}}\right]}$$

Dilution

Dilute ADAKVEO in 0.9% Sodium Chloride Injection or 5% Dextrose Injection, to a total volume of 100 mL for intravenous infusion as follows:

1. Obtain the number of vials required. One vial is needed for every 10 mL of ADAKVEO.
2. Bring vials to room temperature for a maximum of 4 hours prior to the start of preparation (piercing the first vial).
3. Visually inspect the vials.
   - Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit.
   - ADAKVEO is clear to opalescent, colorless or may have a slightly brownish-yellow tint.
   - Do not use if particles are present in the solution.
4. Obtain a 100 mL 0.9% Sodium Chloride Injection or 5% Dextrose Injection infusion bag/container.
   - Infusion bags/containers must be made of either polyvinyl chloride (PVC), polyethylene (PE), or polypropylene (PP).
5. Remove a volume of 0.9% Sodium Chloride Injection or 5% Dextrose Injection from the infusion bag/container that is equal to the required volume of ADAKVEO solution.
6. Withdraw the necessary amount of ADAKVEO solution and dilute by adding to the infusion bag/container containing 0.9% Sodium Chloride Injection or 5% Dextrose Injection.
   - The volume of ADAKVEO added to the infusion bag/container should not exceed 96 mL
7. Gently invert the infusion bag to mix the diluted solution. DO NOT SHAKE.
8. Single-dose vials. Discard unused portion.

Storage Conditions 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

- Administer ADAKVEO diluted solution by intravenous infusion over a period of 30 minutes through an intravenous line, which must contain a sterile, nonpyrogenic 0.2 micron inline filter.
- No incompatibilities have been observed between ADAKVEO and infusion sets composed of PVC, polyethylene (PE- lined PVC), polyurethane (PU), and in-line filter membranes composed of polyethersulfone (PES, neutral and positively charged), positively charged polyamide (PA), and polysulphone (PSU).
- Do not mix or coadminister with other drugs through the same intravenous line.
- After administration of ADAKVEO, flush the line with at least 25 mL of 0.9% Sodium Chloride Injection or 5% Dextrose Injection.
- Dispose of any unused product or waste material in accordance with local requirements.