

PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

This medicine is dispensed with a doctor's prescription only

Darzalex® concentrate for solution for infusion

The active ingredient and its concentration

Daratumumab 20 mg/ml

For a list of the inactive and allergenic ingredients in this preparation – see section 6 “Further Information”. See also “Important information about some of the ingredients of the medicine” in section 2.

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.

Patient Information Card:
In addition to this leaflet, Darzalex is provided with a Patient Safety Information Card. This card contains important safety information you should be aware of and adhere to before starting and during treatment with Darzalex.
Read the Patient Safety Information Card and the patient leaflet before you start using the preparation.
Keep the card for further reading, if necessary.

This medicine has been prescribed for the treatment of your ailment. Do not pass it on to others. It may harm them, even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Darzalex as a monotherapy is intended for the treatment of adult patients (above the age of 18) who have multiple myeloma, which is a cancer of the bone marrow. The treatment is intended for patients with relapsed or refractory disease, in which despite the previous treatment (which includes medicine from the proteasome inhibitor group and immunomodulators), the disease progressed.

Darzalex in combination with lenalidomide and dexamethasone, or in combination with bortezomib and dexamethasone, is intended for the treatment of adult patients with multiple myeloma and who received at least one treatment previously.

Darzalex in combination with bortezomib, melphalan and prednisone is intended for the treatment of adult patients with newly diagnosed multiple myeloma and who are ineligible for autologous stem cell transplant.

The medicine is intended for adults above the age of 18.

Therapeutic group: Monoclonal antibodies. Monoclonal antibodies are proteins designed to recognize and attach to specific targets in the body. Daratumumab has been designed to attach to certain cancer cells in the body, so that the immune system can destroy the cancer cells.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient daratumumab or any of the additional ingredients contained in the medicine Darzalex. For the list of the additional ingredients see section 6 “Further Information”.

Do not use Darzalex if the above applies to you. If you are uncertain, talk to the doctor or nurse before you receive Darzalex.

Special warnings regarding use of the medicine:

Before treatment with Darzalex, refer to the doctor or nurse if:

Infusion-related reactions

Darzalex is given as an infusion (drip) into a vein. Before and after each infusion of Darzalex, you will be given medicines whose purpose is to reduce the risk of infusion-related reactions (see section 3 – “Medicines given during treatment with Darzalex”). These reactions may occur during the infusion or during the 3 days after the infusion.

In some cases, you may have a severe allergic reaction which may be manifested by a swollen face, lips, mouth, tongue or throat, difficulty swallowing or breathing or an itchy rash (hives).

Refer to the doctor or nurse immediately if you have the infusion-related reactions listed in section 4 – “Side Effects”.

If you have infusion-related reactions, you may need additional medicines or you may need to slow down the infusion or stop the infusion. When the reactions arising from the infusion go away or get better, the infusion may be started again.

In most cases these reactions may occur during the first infusion. If you have experienced infusion-related reactions in the past, you are less likely to have these effects a second time.

The doctor may decide not to treat you with Darzalex if you have a severe infusion reaction.

Decreased blood count

Darzalex may cause a decrease in the white blood cell count, which help fight infections, and a decrease in platelets, which help with blood clotting. Please refer to the doctor if you develop fever or signs of bruising or bleeding.

Blood transfusion

If you need a blood transfusion, you need to undergo blood tests to verify your blood type.

Darzalex may affect certain test results (such as the indirect Coombs test) to verify the blood type. Please update the medical staff member who performs the tests that you are being treated with Darzalex.

Children and adolescents

Do not give Darzalex to children or adolescents below the age of 18, as there is no information on how the medicine will affect this population.

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

If you are pregnant, may be pregnant or are planning to become pregnant, refer to the doctor or nurse before beginning treatment with Darzalex.

If you become pregnant during treatment with this medicine, please refer to the doctor or nurse straight away.

A joint decision should be made with the doctor as to whether the benefit of treatment with Darzalex is greater than the risk to the fetus.

Contraception

Women who are being treated with Darzalex should use effective contraception during treatment and for 3 months after treatment.

Breastfeeding

A joint decision should be made with the doctor whether the benefit of breastfeeding is greater than the risk to your baby. The medicine may pass into the mother's milk and it is not known how it will affect the baby.

Driving and using machines

You may feel tired, which may affect your ability to drive or operate machines.

Important information about some of the ingredients of the medicine

The medicine contains sodium:

This medicine contains 9.3 mg sodium (the main component of cooking/table salt) in each 5 ml vial. This is equivalent to 0.46% of the recommended maximum daily intake of sodium for an adult.

This medicine contains 37.3 mg sodium (the main component of cooking/table salt) in each 20 ml vial. This is equivalent to 1.86% of the recommended maximum daily intake of sodium for an adult.

3. HOW SHOULD THE MEDICINE BE USED?

Always use the preparation according to the doctor's instructions.

Check with the doctor or nurse if you are uncertain.

The dosage, treatment regimen and manner of treatment will be determined by the doctor only depending on your body weight.

The usual starting dose of Darzalex is 16 mg per kg of body weight. Darzalex can be given to you as a monotherapy or in combination with other medicines to treat multiple myeloma.

Darzalex is administered as a monotherapy in the following manner:

- once a week for the first 8 weeks
- then, once every 2 weeks, for 16 weeks
- then, once every 4 weeks as long as your condition does not worsen.

When Darzalex is given in combination with other medicines, the doctor may change the time between doses as well as how many treatments you will receive.

Do not exceed the recommended dose

How the medicine is given

Darzalex will be given to you by a doctor or nurse as a drip into the vein over several hours.

Medicines given during treatment with Darzalex

You may be given medicines to lower the chance of getting shingles.

Before each infusion of Darzalex you will be given medicines whose purpose is to reduce the possibility of infusion-related reactions. These medicines may include:

- medicines for an allergic reaction (anti-histamines)
- medicines for inflammation (corticosteroids)
- medicines to reduce fever (such as paracetamol)

After each infusion of Darzalex you will be given medicines (such as corticosteroids) to lower the chance of infusion-related reactions.

Patients with breathing problems

If you have breathing problems, such as asthma or Chronic Obstructive Pulmonary Disease (COPD), you will be given medicines to inhale which will help your breathing problems:

- medicines to help the airways in your lungs stay open (bronchodilators)
- medicines to lower swelling and irritation in your lungs (corticosteroids)

If you received an overdose of Darzalex

This medicine will be given by your doctor or nurse. In the unlikely event that you are given too much (an overdose) your doctor will check you for side effects.

If you missed a scheduled appointment to have Darzalex

It is very important to receive all the prescribed treatments of Darzalex in order for the treatment to work properly. If you miss an appointment for treatment, please make another appointment as soon as possible.

If you have further questions regarding use of the medicine, consult the doctor or nurse.

4. SIDE EFFECTS

As with any medicine, use of Darzalex 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.

Infusion-related reactions

Refer to the doctor or nurse straight away if you experience any of the following effects attributed to the infusion during or in the 3 days after the infusion. You may need other medicines, or the infusion may need to be slowed down or stopped.

These side effects are very common – effects that occur in more than one user in ten

- chills
- sore throat, cough
- nausea
- vomiting
- itchy, runny or blocked nose
- shortness of breath or other breathing problems

Other common side effects – effects that occur in 1-10 in 100 users

- chest discomfort
- dizziness (associated with hypotension)
- itching
- wheezing

Rare side effects – effects that occur in 1-10 in 10,000 users

Severe allergic reaction which may be manifested by a swollen face, lips, mouth, tongue or throat, difficulty swallowing or breathing or an itchy rash (hives).

If you experience any of the infusion-related reactions above, refer to the doctor or nurse straight away.

Other side effects

Very common side effects – effects that occur in more than one user in ten

- fever
- feeling excessively tired
- flu
- diarrhea
- headache
- nerve damage that may cause sensation of slight tingling, numbness and pain
- high blood pressure
- muscle spasms
- swelling of the hands, ankles or legs
- pneumonia
- respiratory tract inflammation – in the nose, sinuses or throat
- low count of red blood cells which carry oxygen in the blood (anemia)
- low count of white blood cells which help fight infections (neutropenia, lymphopenia)
- low count of platelets, blood cells which help with blood clotting (thrombocytopenia)

Common side effects – effects that occur in 1-10 in 100 users

- arrhythmia (atrial fibrillation)
- build-up of fluid in the lungs, making you short of breath

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

Side effects can be reported to the Ministry of Health by clicking on the link “Report Side Effects of Drug Treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects.

5. HOW SHOULD THE MEDICINE BE STORED?

- Darzalex will be stored at the hospital, pharmacy or clinic.
- 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) that appears on the package. The expiry date refers to the last day of that month.
- Store in a refrigerator at 2°C-8°C. Do not freeze.
- Do not shake.
- Store in the original package in order to protect from light.

6. FURTHER INFORMATION

The active substance is daratumumab. Every 1 ml contains 20 mg daratumumab.

Each vial of 5 ml contains 100 mg of daratumumab.

Each vial of 20 ml contains 400 mg of daratumumab.

- In addition to the active ingredient, the medicine also contains: Mannitol, sodium chloride, sodium acetate trihydrate, polysorbate 20, glacial acetic acid, and water for injection.
- **What the medicine looks like and the contents of the package:** Darzalex is a concentrate for solution for infusion. The concentrated solution is colorless to yellow.
- Package size: 1 glass vial of 5 ml or 20 ml in a carton pack

Registration Holder and address: J-C Health Care Ltd., Kibbutz Shefayim 6099000, Israel

Manufacturer's name and address: Cilag AG, Hochstrasse 201, CH-8200 Schaffhausen, Switzerland

This leaflet was checked and approved by the Ministry of Health on: 23.01.2019

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 157-75-34719