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

This medicine is dispensed with a doctor's prescription only

# Darzalex® 20 mg/ml I.V

**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.

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.

Patient Information Card:

In addition to this leaflet, Darzalex 20 mg/ml I.V is provided with a Patient Safety Information Card. This card contains important safety information you should be aware of before starting and during treatment with Darzalex 20 mg/ml I.V, and adhere to.

Read the Patient Safety Information Card and the patient leaflet before you start using the preparation.

Keep the card for further reading, if necessary.

## 1. WHAT IS THE MEDICINE INTENDED FOR?

- Darzalex 20 mg/ml I.V in combination with lenalidomide and dexamethasone, or in combination with bortezomib, melphalan and prednisone, is intended for the treatment of adult patients with newly diagnosed multiple myeloma, which is a cancer of the bone marrow, and who are ineligible for autologous stem cell transplant.
- Darzalex 20 mg/ml I.V in combination with bortezomib, thalidomide and dexamethasone is intended for the treatment of adult patients with newly diagnosed multiple myeloma, who are eligible for autologous stem cell transplant.
- Darzalex 20 mg/ml I.V 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 20 mg/ml I.V as a monotherapy is intended for the treatment of adult patients (above the age of 18 years) who have multiple myeloma. The treatment is intended for patients with relapsed and refractory disease, in whom despite the previous treatment (which includes medicines from the proteasome inhibitor group and immunomodulators), the disease progressed.

**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 20 mg/ml I.V. For the list of the additional ingredients, see section 6 "Further Information".

Do not use Darzalex 20 mg/ml I.V if the above applies to you. If you are uncertain, talk to the doctor or nurse before you receive Darzalex 20 mg/ml I.V.

**Special warnings regarding use of the medicine**

**Before treatment with Darzalex 20 mg/ml I.V, refer to the doctor or nurse in the following situations:**

Infusion-related reactions

Darzalex 20 mg/ml I.V is given as an infusion (drip) into a vein. Before and after each infusion of Darzalex 20 mg/ml I.V , 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 20 mg/ml I.V"). 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). Some cases of serious allergic reactions or other severe infusion-related side effects have resulted in death.

Refer to the doctor or nurse immediately if you have the infusion-related reactions or related symptoms listed at the top of section 4 – "Side Effects".

If you have infusion-related reactions, you may need additional medicines or the infusion may need to be slowed down or stopped. 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 20 mg/ml I.V if you have a severe infusion reaction.

Decreased blood count

Darzalex 20 mg/ml I.V may cause a decrease in the white blood cell count, which help fight infections, and a decrease in platelet count, which help with blood clotting. Please refer to the doctor or nurse if you develop symptoms of infection such as fever or symptoms of decreased platelet counts such as bruising or bleeding.

Blood transfusion

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

Darzalex 20 mg/ml I.V 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 20 mg/ml I.V.

Hepatitis B

Tell your doctor if you have a hepatitis B infection or have had in the past. This is because Darzalex 20 mg/ml I.V could cause the hepatitis B virus to become active again. Your doctor may check you for signs of this infection before, during and for some time after treatment with Darzalex 20 mg/ml I.V. Tell your doctor right away if you notice worsening tiredness or yellowing of your skin or whites of your eyes.

**Children and adolescents**

This medicine is not intended for children and adolescents below the age of 18.

There is no information regarding the safety and effectiveness of this preparation in children and adolescents.

**Drug interactions**

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

**Pregnancy, breastfeeding and fertility**

**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 20 mg/ml I.V.

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 20 mg/ml I.V is greater than the risk to the fetus.

**Contraception**

Women who are being treated with Darzalex 20 mg/ml I.V 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**

After treatment with Darzalex 20 mg/ml I.V, 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 regarding the dosage and treatment regimen of the preparation.

The dosage, treatment regimen and manner of treatment with Darzalex 20 mg/ml I.V will be determined by the doctor only, depending on your body weight.

The usual starting dose of Darzalex 20 mg/ml I.V is 16 mg per kg of body weight. Darzalex 20 mg/ml I.V can be given to you as a monotherapy or in combination with other medicines to treat multiple myeloma.

Darzalex 20 mg/ml I.V 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 20 mg/ml I.V is given in combination with other medicines, the doctor may change the time between doses as well as how many treatments you will receive.

In the first week, the doctor may give you the Darzalex 20 mg/ml I.V dose split over two consecutive days.

**Do not exceed the recommended dose.**

**How the medicine is given**

Darzalex 20 mg/ml I.V 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 20 mg/ml I.V**

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

Before each infusion of Darzalex 20 mg/ml I.V 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 20 mg/ml I.V 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 20 mg/ml I.V**

Darzalex 20 mg/ml I.V will be given to you by your doctor or nurse; therefore, it is unlikely that you will

receive an overdose. Your doctor will check you for side effects.

**If you missed a scheduled appointment to have Darzalex 20 mg/ml I.V**

It is very important to receive all the prescribed treatments of Darzalex 20 mg/ml I.V in order for the treatment to work properly. If you miss an appointment for treatment, 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 20 mg/ml I.V 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 include the following symptoms:

**Very common side effects** – effects that may affect more than 1 in 10 users:

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

**Common side effects** – effects that may affect up to 1 in 10 users:

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

**Rare side effects** – effects that may affect up to 1 in 1,000 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). See section 2 “Before using the medicine”.
- eye pain
- blurred vision

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 may affect more than 1 in 10 users:

- fever
- feeling excessively tired
- diarrhea
- constipation
- decreased appetite
- headache
- nerve damage that may cause sensation of slight tingling, numbness or pain
- high blood pressure
- muscle spasms
- swelling of the hands, ankles or feet
- weakness
- back pain
- chills
- pneumonia
- bronchitis
- respiratory tract inflammation – e.g., 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, leukopenia)
- low count of platelets, blood cells which help with blood clotting (thrombocytopenia)
- unusual feeling in the skin (such as a tingling or a feeling of “pins and needles” in the skin)

**Common side effects** – effects that may affect up to 1 in 10 users:

- arrhythmia (atrial fibrillation)
- build-up of fluid in the lungs, making you short of breath
- flu
- urinary tract infection
- severe infection throughout the body (sepsis)
- dehydration
- fainting
- high level of sugar in the blood
- low level of calcium in the blood
- low level of antibodies called immunoglobulins in the blood, which help fight infections (hypogammaglobulinemia)
- inflamed pancreas
- type of herpes virus infection (cytomegalovirus infection)
- coronavirus disease (COVID-19)

**Uncommon side effects** – effects that may affect up to 1 in 100 users:

- inflamed liver (hepatitis)

**If a side effect occurs, 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, or by entering the link:

https://sideeffects.health.gov.il

## 5. HOW SHOULD THE MEDICINE BE STORED?

- Darzalex 20 mg/ml I.V 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 20 mg/ml I.V 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.

Manufacturer: Cilag AG, Hochstrasse 201, CH-8200, Schaffhausen ,Switzerland.

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

Revised in February 2023 according to MOH guidelines.

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