Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986
This medicine is dispensed with a doctor's prescription only

ELREXFIO®
Solution for subcutaneous injection

The active ingredient is elranatamab 40 mg/ml
- A 1.1 ml vial contains 44 mg of elranatamab
- A 1.9 ml vial contains 76 mg of elranatamab

Inactive ingredients and allergens: See section 2 under 'Important information about some of this medicine's ingredients' and section 6 'Further information'.

Read the entire leaflet carefully before using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult your 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 to yours.

In addition to the patient information leaflet, ELREXFIO also has a patient safety information card.
This card contains important safety information that you need to know and that you should follow before starting treatment and during treatment with ELREXFIO.
Carefully read the patient safety information card and patient information leaflet before you start using this medicine. Keep the card in case you need to read it again.

1. WHAT IS THIS MEDICINE INTENDED FOR?

ELREXFIO is indicated as monotherapy for the treatment of adult patients with relapsed and refractory multiple myeloma, who have received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody and have demonstrated disease progression on the last therapy.

Therapeutic group: Monoclonal antibodies and antibody–drug conjugates.

ELREXFIO is an antibody, a type of protein, which has been designed to recognise and attach to specific targets in your body. ELREXFIO targets BCMA (B-cell maturation antigen), which is found on multiple myeloma cancer cells, and the CD3 (cluster of differentiation 3) receptor, which is found on a particular kind of white blood cells in your immune system called T lymphocytes. This medicine works by attaching to these cells and bringing them together, which helps your immune system cells destroy the multiple myeloma cancer cells.

2. BEFORE USING THIS MEDICINE

Do not use ELREXFIO if:
- You are sensitive (allergic) to the active ingredient or to any of the other ingredients in this medicine (listed in section 6).
  If you are not sure if you are sensitive (allergic), contact your doctor or nurse before receiving the medicine.

Special warnings regarding use of the medicine
Tell your doctor or nurse about all of your medical conditions before you are given ELREXFIO, including if you have had any recent infections.

Look out for serious side effects.

Tell your doctor or nurse right away if you experience any of the following:
- Signs of a condition known as ‘cytokine release syndrome’ (CRS). CRS is a serious immune reaction with symptoms such as fever, difficulty breathing, chills, headache, low blood pressure, fast heartbeat, dizziness, and increased levels of liver enzymes in the blood.
- Effects on your nervous system. Symptoms include feeling confused, feeling less alert, or having difficulty speaking or writing. Some of these symptoms may be signs of a serious immune reaction called ‘immune effector cell-associated neurotoxicity syndrome’ (ICANS).
- Signs and symptoms of an infection such as fever, chills, fatigue, or difficulty breathing.

Tell your doctor or nurse if you notice any of the above signs.

ELREXFIO and vaccines
Before treatment with ELREXFIO, tell your doctor or nurse if you have had a recent vaccination or if you are planning to have a vaccination. You should not receive live vaccines within the four weeks before your first dose, during the treatment, and at least until four weeks after stopping treatment with ELREXFIO.

Children and adolescents
This medicine is not intended for children or adolescents below 18 years of age.

Tests and follow-up
Before treatment with ELREXFIO, your doctor will check your blood counts for signs of infection. If you have any infection, it will be treated before you start receiving ELREXFIO. Your doctor will also check if you are pregnant or breastfeeding.

During treatment with ELREXFIO, your doctor will monitor you for side effects. Your doctor will monitor you for signs and symptoms of CRS and ICANS for 48 hours after each of your first two doses of ELREXFIO. Your doctor will also regularly check your blood counts, as the number of blood cells and other blood components may decrease.

Drug interactions
If you are taking or have recently taken, other medicines, including nonprescription medicines and dietary supplements, tell your doctor or pharmacist. Particularly if you are taking medicines such as cyclosporine, phenytoin, sirolimus, and warfarin.

Pregnancy and breastfeeding
It is not known if ELREXFIO affects an unborn baby or if it passes into breast milk.

<u>Pregnancy information for women</u>
ELREXFIO administration is not recommended during pregnancy.
Tell your doctor or nurse before receiving ELREXFIO if you are pregnant, think you are pregnant or plan to become pregnant.
If you can become pregnant, your doctor will request a pregnancy test before starting treatment.
If you become pregnant while being treated with the medicine, tell your doctor or nurse straight away.
ELREXFIO is associated with hypogammaglobulinemia, therefore, assessment of immunoglobulin levels in newborns of mothers treated with ELREXFIO should be considered.

Contraception
If you can become pregnant, you must use effective contraception during treatment and for 6 months after stopping treatment with ELREXFIO.

Breastfeeding
You should not breastfeed during treatment and for 6 months after stopping treatment with ELREXFIO.

Driving and using machines
The medicine has a significant effect on the ability to drive or operate machines.
Some people may feel tired, dizzy, or confused during treatment with ELREXFIO. Do not drive, use tools, or operate machines until at least 48 hours after each of your first 2 doses, and until your symptoms improve, or as instructed by your doctor.

Important information about some of this medicine's ingredients
ELREXFIO contains less than 1 mmol (23 mg) sodium per dose, that is to say essentially 'sodium-free'.

3. HOW TO USE THIS MEDICINE?

Always use this medicine according to your doctor's instructions. Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the medicine.
The dosage and treatment regimen will be determined by your doctor only.
The standard dosage of ELREXFIO is usually: 76 mg, but the first two doses will be lower.

ELREXFIO is given as follows:
- You will receive a first dose of 12 mg on Day 1 of Week 1.
- You will receive a second dose of 32 mg on Day 4 of Week 1.
- From Week 2 to Week 24 (Day 1), you will receive a dosage of 76 mg once a week, as long as you are getting benefit from ELREXFIO.
- From Week 25 onwards, your doctor may change your treatment from once a week to once every two weeks, as long as your disease responds to ELREXFIO treatment.

Do not exceed the recommended dose.

You should stay close to a healthcare facility for 48 hours after each of the first two doses in case you experience side effects. Your doctor will monitor you for side effects for 48 hours after each of your first two doses.

How the medicine is given
ELREXFIO will always be given to you by your doctor or nurse as an injection under your skin (subcutaneous). It is given in the stomach area or thigh.

You may get a reaction at the injection site, including redness of the skin, pain, swelling, bruising, rash, itching, or bleeding. These effects are usually mild and resolve by themselves with no need for any additional treatment.

Additional medicines given during treatment with ELREXFIO
You will be given medicines one hour before each of your first three doses of ELREXFIO. These will help to lower the chance of side effects, such as cytokine release syndrome (CRS) (see section 4). These medicines may include:

- Medicines to reduce the risk of fever (such as paracetamol)
- Medicines to reduce the risk of inflammation (corticosteroids)

- Medicines to reduce the risk of an allergic reaction (antihistamines, such as diphenhydramine)

You may also be given these medicines before later doses of ELREXFIO based on any symptoms you experience after receiving the medicine.

You may also be given additional medicines based on any symptoms you experience or your medical history.

If you receive an overdose of ELREXFIO
This medicine will be given by your doctor or nurse; it is unlikely that you receive too much. In case you receive more than you should (an overdose), your doctor will check you for side effects.

If you miss your appointment to receive ELREXFIO
It is very important to attend all your appointments to make sure that your treatment is effective. If you miss an appointment, schedule another one as soon as possible.

Adhere to the treatment as recommended by your doctor.

Even if your health improves, do not stop treatment with this medicine without consulting your doctor.

Do not take medicines in the dark! Check the label and dose each time you take medicine. Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of ELREXFIO may cause side effects in some users. Do not be alarmed by this list of side effects; you may not experience any of them.

Serious side effects
Get medical help straight away if you develop any of the following serious side effects, which may be severe and fatal.

Very common side effects (may affect more than 1 in 10 people):
- 'Cytokine release syndrome' (CRS). A serious immune reaction that may cause fever, difficulty breathing, chills, dizziness, fast heartbeat, increased liver enzymes in the blood
- Low level of white blood cells (neutropenia)
- Low level of antibodies called ‘immunoglobulins’ (hypogammaglobulinemia), which may make infections more likely
- Infection, which may include fever, chills, fatigue, or difficulty breathing

Common side effects (may affect up to 1 in 10 people):
- A serious immune reaction called 'immune effector cell-associated neurotoxicity syndrome' (ICANS), that may cause effects on your nervous system. Some of the symptoms are:
  - Feeling confused
  - Feeling less alert
  - Having difficulty speaking or writing

Tell your doctor or nurse right away if you notice any of the above-listed serious side effects.

Additional side effects
Additional side effects are listed below. Tell your doctor or nurse if you develop any of these side effects.

Very common side effects (may affect more than 1 in 10 people):
- Low levels of red blood cells (anemia)
- Feeling tired or weak
- Nose and throat infection (upper respiratory tract infection)
- Reactions at or near the injection site, including redness of the skin, itching, swelling, pain, bruising, rash, or bleeding
- Diarrhea
- Lung infection (pneumonia)
- Low levels of blood platelets (cells that help blood to clot; thrombocytopenia)
- Low levels of lymphocytes, a type of white blood cell (lymphopenia)
- Fever (pyrexia)
- Decreased appetite
- Skin rash
- Dry skin
- Pain in your joints (arthralgia)
- Low levels of potassium in the blood (hypokalemia)
- Nausea (Feeling sick)
- Headache
- Difficulty breathing (dyspnea)
- Blood poisoning (sepsis)
- Low number of white blood cells (leucopenia)
- Increased level of liver enzymes in the blood (transaminases increased)
- Nerve damage in legs and/or arms that may cause tingling, numbness, pain, or loss of sensation (peripheral neuropathy)
- Urinary tract infection

Common side effects (may affect up to 1 in 10 people):
- Low level of phosphates in the blood (hypophosphatemia)
- Low number of neutrophils in the blood, accompanied by fever (febrile neutropenia)

If you experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

You can report side effects to the Ministry of Health by following the link ‘Reporting Side Effects of Drug Treatment' on the Ministry of Health home page (www.health.gov.il) which links to an online form for reporting side effects or by using the link: https://sideeffects.health.gov.il

5. HOW TO STORE THE MEDICINE?

- Prevent poisoning! This and any other medicine should be kept in a closed place, out of the reach and sight of children and/or infants to avoid poisoning.
- Do not use the medicine after the expiry date (exp. date) which is stated on the package. The expiry date refers to the last day of that month.
  Storage conditions:
- The medicine will be stored at the hospital or clinic by your doctor.
- Store in a refrigerator (2°C- 8°C). Do not freeze.

- Store in the original carton to protect from light.
- Do not use this medicine if you notice discoloration or other visible signs of deterioration.

6. FURTHER INFORMATION

In addition to the active ingredient, this medicine also contains:
Sucrose, L-histidine hydrochloride monohydrate, L-histidine, polysorbate 80, edetate disodium, water for injection.

What the medicine looks like and contents of the pack:
Solution for injection (injection), a colorless to pale brown liquid.
Supplied in two strengths. Each pack contains one glass vial.

Registration holder and address: Pfizer Pharmaceuticals Israel Ltd., 9 Shenkar St., Herzliya Pituach 46725.

Registration number of the medicine in the Ministry of Health National Drug Registry:
177-77-37990

Approved in 12/2024

Instructions for healthcare professionals:
ELREXFIO 40 mg/mL solution for injection is supplied as ready-to-use solution that does not need dilution prior to administration. Do not shake.

ELREXFIO is a clear to slightly opalescent, and colorless to pale brown solution. The solution should not be administered if it is discolored or contains particulate matter.

Aseptic technique should be used to prepare and administer ELREXFIO.

Preparation instructions

ELREXFIO 40 mg/mL solution for injection vials are for single use only.

ELREXFIO should be prepared following the instructions below (see Table 1) depending on the required dose. It is suggested to use a 44 mg/1.1 mL (40 mg/mL) single dose vial for each one of the step-up doses.

Table 1. Preparation instructions for ELREXFIO

Required dose	Dose volume
12 mg (Step-up dose 1)	0.3 mL
32 mg (Step-up dose 2)	0.8 mL
76 mg (Full treatment dose)	1.9 mL

Once punctured, the vial and dosing syringe should be used immediately. If the prepared dosing syringe is not used immediately, store syringe between 2°C to 30°C for a maximum of 24 hours.

Administration instructions

ELREXFIO is for subcutaneous injection only and should be administered by a healthcare professional.

The required dose of ELREXFIO should be injected into the subcutaneous tissue of the abdomen (preferred injection site). Alternatively, ELREXFIO may be injected into the subcutaneous tissue of the thigh.

ELREXFIO for subcutaneous injection should not be injected into areas where the skin is red, bruised, tender, hard, or areas where there are scars.

Traceability

In order to improve the traceability of biological medicinal products, the name and the batch number of the administered product should be clearly recorded.

Disposal

The vial and any remaining contents should be discarded after a single use. Any unused medicinal product or waste material should be disposed of in accordance with local requirements.