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

The medicine is dispensed with a doctor's prescription only.

Alkeran Tablets 2 mg

Each tablet contains: Melphalan 2 mg.

Inactive ingredients and allergens in the preparation - see section 6.

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 to treat 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?

To treat multiple myeloma and ovarian adenocarcinoma (advanced stage).

Therapeutic group: Nitrogen mustard analogs.

2. BEFORE USING THE MEDICINE:

☒ Do not use the medicine if:
- You are sensitive (allergic) to the active ingredient or to any of the other components of the medicine.

Special warnings regarding use of the medicine

❗ Before treatment with Alkeran, tell the doctor if:
- You are undergoing, or have recently undergone, chemotherapy or radiotherapy.
- You have a kidney problem.

If you are uncertain if one of the above applies to you, consult the doctor or pharmacist before taking the medicine.

❗ If you are taking, or have recently taken, other medicines, including non-prescription medicines, nutritional supplements and herbal preparations, tell the doctor or pharmacist. Especially inform the doctor or pharmacist if you are taking:
- Other cytotoxic drugs (chemotherapy).
- Nalidixic acid (an antibiotic used to treat urinary tract infections).
- Ciclosporin (used to prevent rejection of organs or tissues following a transplant or to treat certain skin conditions such as psoriasis and eczema or to treat rheumatoid arthritis).

❗ Use of the medicine and vaccination

If you are planning to be vaccinated, consult the doctor or medical staff before receiving the vaccination. This is because some vaccines (e.g., polio, measles, mumps and rubella) may give you an infection while using Alkeran.

❗ Fertility

Do not use Alkeran if you plan to have children. This warning applies to both men and women.
- In women, Alkeran may cause the ovaries to stop producing oocytes and to stop the menstrual cycle.
- In men, Alkeran may cause a temporary or permanent decrease in sperm count due to suppression of testicular function.

Use a reliable contraceptive to prevent pregnancy if you or your partner are taking Alkeran. Refer to the doctor for advice.

❗ Pregnancy and breastfeeding

Treatment with Alkeran is not recommended during pregnancy as it may cause irreversible damage to the unborn baby. If you become pregnant, think you became pregnant or are planning to become pregnant in the future, consult the doctor before using Alkeran. The doctor will weigh the risks and the benefits to you and your baby in taking Alkeran.
Do not breastfeed when using Alkeran. Refer to the doctor for advice.

3. HOW SHOULD YOU USE THE MEDICINE?

Alkeran must only be prescribed for you by a doctor specializing in blood problems or cancer.
Always use according to the doctor's instructions.
Check with the doctor or pharmacist if you are uncertain.
The dosage and treatment regimen will be determined by the doctor only.
It is important to be sure to take the medicine at the appropriate times.
- Swallow the medicine whole with a glass of water.
- **Do not break, crush or chew the tablets. The product is cytotoxic.**

The Alkeran dosage depends on the blood problem or cancer type you have (see section 1).
Do not exceed the recommended dose.
The doctor may change the dosage during the course of treatment, as needed. Sometimes, the dosage can change if you are elderly or you have a kidney problem.

Tests and follow-up: During the course of treatment with Alkeran, the doctor will perform routine blood tests. This is to check your blood cell count. As a result, the doctor may change the dosage.

If you accidentally take a higher dosage

If you took an overdose, or if a child has accidentally swallowed the medicine, immediately refer to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forget to take the medicine

If you forgot to take this medicine at the required time, refer to the doctor. **Do not take a double dose to compensate for a forgotten one.**
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 or pharmacist.
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 further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

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

Refer immediately to a specialist doctor or to the hospital if any of the following symptoms occur:
- Allergic reaction, the symptoms of which may include:
  - A rash, lumps or hives on the skin.
  - Swelling of the face, eyelids or lips.
  - Sudden wheezing and tightness of the chest.
  - Collapse (due to cardiac arrest).
- Signs of high fever or infection (sore throat, sore mouth or urinary tract problems). Treatment with Alkeran may cause reduced white blood cell counts. White blood cells fight infection and when there are too few of them, infections can occur.
- Any **unexpected** bruising or **unexpected** bleeding or extreme tiredness, dizziness or breathlessness, as this may indicate inadequate production of certain blood cells.
- If you **suddenly** feel unwell (even without fever).

Additional side effects
Consult the doctor if you have any of the following side effects:

Very common side effects that occur in more than 1 in 10 users
- A drop in the number of blood cells and platelets.
- Feeling sick (nausea), being sick (vomiting) and diarrhea.
- Mouth ulcers - with high dosages of Alkeran.
- Hair loss - with high dosages of Alkeran.

Common side effects that occur in 1-10 of 100 users
- Hair loss - with usual dosages of Alkeran.
- High levels of urea in the blood – in people with kidney problems who are being treated for myeloma.

Rare side effects that occur in 1-10 of 10,000 users
- An illness in which you have a low number of red blood cells as they are being destroyed prematurely – this can make you feel very tired, breathless and dizzy and can give you headache or cause jaundice (yellowing of the whites of the eyes and skin).
- Lung problems which may cause coughing or wheezing and make breathing difficult.
- Liver problems which may show up in blood tests or cause jaundice (yellowing of the whites of the eyes and skin).
- Mouth ulcers – with normal dosages of Alkeran.
- Skin rashes or itching skin.

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

Use of Alkeran may, in the future, cause a certain type of cancer called secondary acute leukemia. This cancer causes the bone marrow (the tissue in the bone that produces red and white blood cells) to produce large numbers of cells that function improperly. The symptoms of this condition include: fatigue, fever, infections and hematomas. This condition may show up in your blood tests which will show that there are many blood cells that are not working properly and too few cells that work normally.
Refer to the doctor as soon as possible if any of the symptoms occur. You may have to discontinue treatment, but this should only be done upon the doctor's instruction.

Reporting side effects:
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://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il
In addition, you can report to Perrigo via the following address: www.perrigo-pharma.co.il

5. HOW SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be kept in a safe place out of the sight and reach of children and/or infants 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 carton and label. The expiry date refers to the last day of that month.
- Store refrigerated (2°C-8°C).
  Can be used for 60 days after first opening, but not later than the expiry date.
- If your doctor tells you to stop the treatment, it is important that you return the remaining medicine to the pharmacist so he can dispose of it as per the guidelines for disposal of hazardous materials. Only keep the remaining medicine upon explicit instruction from the doctor.

6. FURTHER INFORMATION

- In addition to the active ingredient, the medicine also contains:
  Microcrystalline cellulose, opadry white YS-1-18097-A (hypromellose, titanium dioxide, macrogol), crospovidone, magnesium stearate, colloidal anhydrous silica.
- What the medicine looks like and the contents of the package: Alkeran is packaged in a dark glass bottle with a plastic cap that contains 25 white to off-white, round, biconvex tablets. Each tablet is engraved with 'GXEH3' on one side and 'A' on the other side.
- Registration holder: Perrigo Israel Agencies Ltd., 1 Rakefet St., Shoham.
- Manufacturer: Excella GmbH&Co. KG, Feucht, Germany, for Aspen.
- This leaflet was checked and approved by the Ministry of Health in June 2014.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 12955.30948