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

Active ingredient and its quantity:
Each tablet contains: Melphalan 2 mg

Inactive ingredients and allergens in the preparation - see section 6 "Further Information" in the leaflet.

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 illness. Do not pass it on to others. It may harm them even if it seems to you that their illness is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Alkeran Tablets 2 mg is intended for the treatment of multiple myeloma and ovarian adenocarcinoma (advanced stage).

Therapeutic group: The medicine belongs to the group of cytotoxic medicines (also called chemotherapy), antineoplastic and immunomodulatory factors, alkylating agents and nitrogen mustard analogs.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:
- You are sensitive (allergic) to the active ingredient melphalan or to any of the other ingredients of this medicine (see section 6 "Further Information").
- You are breastfeeding.

If you are not sure, refer to the doctor or pharmacist before taking 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.
- You are going to have a vaccination or were recently vaccinated. This is because some vaccines (like polio, measles, mumps and rubella) may give you an infection if you have them whilst you are using Alkeran Tablets 2 mg.
- You are using combined oral contraception (the Pill). This is because of the increased risk of venous thromboembolism (a blood clot that forms in a vein and migrates to another location) in patients with multiple myeloma.

Alkeran Tablets 2 mg could increase the risk of developing other types of cancer (e.g., secondary solid tumours) in a small number of patients, particularly when used in combination with lenalidomide, thalidomide and prednisone. Your doctor should carefully evaluate the benefits and risks when you are prescribed Alkeran.
If you are uncertain if one of the above applies to you, consult the doctor or pharmacist before taking the medicine.

Drug interactions
If you are taking, or have recently taken, other medicines, including non-prescription medicines, nutritional supplements and herbal preparations, tell the doctor. Especially inform the doctor if you are taking:
- Vaccines which contain live organisms (see Warnings section).
- 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).
- In children, busulfan (another chemotherapeutic medicine used to treat certain type of cancers).

Pregnancy, breastfeeding and fertility
Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you may be pregnant or are planning a pregnancy, consult the doctor or pharmacist before using the medicine.
Treatment with Alkeran is not recommended during pregnancy because it may cause permanent damage to a foetus.
Do not take Alkeran if you are planning to have a baby. This warning applies to both men and women.
Use a reliable contraceptive to prevent pregnancy if you or your partner are taking these tablets.
If you are already pregnant, it is important to talk to your doctor before taking Alkeran.
The doctor will consider 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.

Fertility
Melphalan can affect ovaries or sperm, which may cause infertility (inability to have a baby). In women, menstruation can stop (amenorrhoea) and in men, a complete lack of sperm may be observed (azoospermia). Due to the possibility of the lack of sperm as a result of Alkeran treatment, it is advised for men to have a consultation on sperm preservation before treatment. It is recommended that men who are receiving treatment with Alkeran not father a child during treatment and up to 6 months afterwards.

Driving and using machines
Effects on the ability to drive and operate machinery in patients taking the medicine have not been studied.

3. HOW SHOULD YOU USE THE MEDICINE?

Alkeran must only be prescribed for you by a doctor specializing in cancer.
Alkeran is an active cytotoxic preparation for use under the direction of doctors experienced in the administration of such medicines.
Always use the preparation according to the doctor's instructions.
Check with the doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the preparation.
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.
The label on your package will indicate how many tablets to take and how often to take them.
If the label doesn't say or if you are not sure, ask the doctor or pharmacist.
- Swallow the medicine whole with a glass of water.
- **Do not break, crush or chew the tablets.**

The Alkeran dosage depends on the type of blood problem or cancer 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 or someone else 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 stop taking the medicine
If you have further questions on the use of this 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).
- Any 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).
- If you experience any of the symptoms/signs which can be related to a thromboembolic event (such as shortness of breath, chest pain, arm or leg swelling) especially if you are treated with Alkeran in combination with lenalidomide and prednisone or thalidomide and prednisone or dexamethasone.

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 - with high doses of Alkeran.
- 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 a chemical called 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 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.

Side effects of unknown frequency (effects whose frequency has not been determined yet)
- Leukaemia - cancer of the blood.
- In women - menstrual periods stop (amenorrhoea).
- In men - absence of sperm in the semen (azoospermia).
- Deep vein thrombosis and pulmonary embolism.

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 increase the risk of developing a different type of cancer called secondary acute leukemia (blood cancer) in the future. This type of cancer causes the bone marrow (the tissue in the bone that produces red and white blood cells) to produce a large number 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 with Alkeran, 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://sideeffects.health.gov.il
In addition, you can report to Padagis via the following address:
Padagis.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 reach and sight 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.
- Do not discard medicines via wastewater or household waste. Ask the pharmacist how to dispose of medicines that are not in use. These measures will help protect the environment.

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, film-coated tablets. Each tablet is engraved with 'GX EH3' on one side and 'A' on the other side.
- Registration holder: Padagis Israel Agencies Ltd., 1 Rakefet St., Shoham.
- Manufacturer: Excella GmbH & Co. KG, Feucht, Germany, for Aspen.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 12955.30948
- Revised in November 2022 according to MOH guidelines.