PATIENT PACKAGE INSERT ACCORDING TO PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Leukeran Tablets 2 mg

The active ingredient and its quantity:
Each tablet contains: Chlorambucil 2 mg
Inactive ingredients and allergens in the medicine – see section 6 in the leaflet.

Read this entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine.
If you have any further questions, refer to the doctor or pharmacist.
This medicine is prescribed for you. 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?

Leukeran is used to treat Hodgkin's disease, indolent non-Hodgkin's lymphoma, chronic lymphocytic leukaemia and Waldenstrom's macroglobulinaemia.

Therapeutic group: The medicine belongs to a group of medicines called cytotoxics (also called chemotherapy), antineoplastic and immunomodulatory agents,
Alkylating agents – nitrogen mustard analogues.

2. BEFORE USING THE MEDICINE

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

If you are not sure, refer to the doctor before taking the medicine.

Special warnings regarding the use of this medicine
Before treatment with Leukeran, tell the doctor if:
- You were recently vaccinated or are planning to receive a vaccine containing live organisms (see the section regarding combining other medicines with Leukeran). Leukeran may cause your body to be less capable of fighting infections.
- You are a potential candidate for a bone marrow transplant (autologous stem cell transplantation), as prolonged use of the medicine may reduce the number of stem cells.
- You are undergoing or have recently undergone chemotherapy or radiotherapy.
- You have liver or kidney problems.
- You have a kidney problem (nephrotic syndrome), had high pulse dosing regimen or if you have had a fit or convulsions. If you have ever had fits or convulsions, there may be an increased risk for fits or convulsions while using Leukeran.

The use of Leukeran may increase the risk of developing secondary types of blood cancer, primarily in long-term use. In many cases, patients who develop this have also received other chemotherapy or radiotherapy. The symptoms of secondary blood cancer include: tiredness, fever, infections and bruising.
Refer to the doctor as soon as possible if one of these side effects appears (see section 4).
If you are not sure if any of sections above apply to you, consult with the doctor, medical staff or pharmacist before taking the medicine.

Drug interactions
If you are taking, or have recently taken, or planning to take other medicines including nonprescription medicines, nutritional supplements and herbal remedies, tell the doctor or pharmacist. Particularly inform the doctor or pharmacist if you are taking or have recently taken:
- Vaccines which contain live organisms (such as an oral polio vaccine, measles, mumps, rubella).
- Fludarabine, pentostatin or cladribine – medicines used during chemotherapy to treat hematological malignancies (types of cancer that affect blood, bone marrow and lymph nodes).

Use of this medicine and food
Take the medicine on an empty stomach. See section 3 "How should you use this medicine?".

Pregnancy, breastfeeding and fertility
Pregnancy and breastfeeding
If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, consult the doctor before using Leukeran.
Do not use Leukeran if you intend to have children. This warning applies to both men and women.
Treatment with Leukeran is not recommended during pregnancy because it might cause irreversible damage to the fetus. The doctor will consider the risks and benefits to you and your fetus resulting from the use of Leukeran.
Do not breastfeed while using Leukeran. There are reports that Leukeran and its ingredients can be passed into breast milk.
Consult with the doctor.
Fertility
Leukeran can affect the ovaries or sperm cells and cause infertility (inability to have children). The menstrual cycle might stop in women (amenorrhoea) and in men there might be a condition of lack of sperm cells (azoospermia). Use reliable contraception to avoid pregnancy if either you or your partner are taking Leukeran. Consult with the doctor.

Driving and operating machinery
There is no information on the effects of Leukeran on the ability to drive or operate machinery.

Important information about some of the ingredients of this medicine
The medicine Leukeran contains lactose. If the doctor has told you that you are sensitive to certain sugars, refer to the doctor before using the medicine.

3. HOW SHOULD YOU USE THIS MEDICINE?

Always use the medicine according to the doctor's instructions. You should check with the doctor or pharmacist if you are not sure about the dosage and manner of treatment with the medicine. The dosage and manner of treatment will be determined by the doctor only.
Leukeran should only be administered by a specialist doctor in cancer treatment.
The duration of treatment will be determined only by the doctor based on your disease.
- Leukeran is administered orally. Take the medicine each day on an empty stomach (at least an hour before a meal or 3 hours after a meal).
- Swallow the tablet whole with a glass of water.
- **It is forbidden to halve, break, crush or chew the tablets. This product is cytotoxic.**

Do not exceed the recommended dose.
The dosage of Leukeran depends on the type of your blood problem or cancer (see section 1).
- The doctor may change the dosage during treatment, as necessary. Sometimes the dosage can change if you are an elderly person or have liver problems. If you are an elderly person, it may be necessary to monitor your kidney or liver function during treatment.
- During the treatment with Leukeran the doctor will perform regular blood tests to check your blood cell count. As a result, the doctor may change the dosage.

If you have accidentally taken a higher dosage
If you took an overdose or if a child or someone else accidentally swallowed the medicine, refer immediately to a doctor or a hospital emergency room and bring the package of the medicine with you.

If you forgot to take the medicine
If you forgot to take this medicine at the scheduled time, refer to the doctor. **Do not take a double dose to make up for a forgotten dose.**
Continue with the treatment as 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 the dose each time you take a medicine. Wear glasses if you need them.

If you stop taking the medicine
If you have further questions regarding the use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, the use of Leukeran 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 the specialist doctor or hospital if any of these symptoms appear:
- Signs of high fever or infection (sore throat, sore mouth or problems in the urinary tract).
- The appearance of **unexpected** bruising or bleeding, as this may indicate reduced production of certain blood cells.
- If you **suddenly** feel unwell (even without fever).
- If you start feeling extremely tired.
- If you notice muscle numbness or weakness.
- If you notice skin rashes, blisters on the skin, sore mouth or eyes and you have a high temperature.

Additional side effects
Consult the doctor if any of the following side effects appear:
Very common side effects that appear in more than 1 out of 10 users:
- A reduced blood cell count and bone marrow suppression.

Common side effects that appear in less than 1 out of 10 users:
- Nausea, vomiting, diarrhea or mouth ulcers.
- Secondary types of blood cancer (acute secondary hematologic malignancies).
- Fits (convulsions) in children with a kidney problem known as nephrotic syndrome.
- A reduced red blood cell count or anemia that may cause tiredness, weakness or shortness of breath.

Uncommon side effects that appear in less than 1 out of 100 users:
- Rash.

Rare side effects that appear in less than 1 out of 1,000 users:
- Yellowing of the whites of the eyes or skin (jaundice).
- Symptoms of allergic reactions such as skin lumps, hives or swelling of the tissues (edema).
- In rare cases, skin rash that developed into serious conditions, including Stevens-Johnson syndrome and toxic epidermal necrolysis, has been reported. These two forms of the same serious skin disease cause rash, skin peeling and sores on the mucous membranes.
- Fever.
- Fit or convulsion.
- Liver damage or injury (hepatotoxicity).

Very rare side effects that appear in less than 1 out of 10,000 users:
- Abnormal repetitive shaking movements of the body or twitching, without fits or convulsions.
- Inflammation of the bladder called cystitis.
- Irreversible bone marrow failure – your body may stop producing blood cells transiently.
- Scarring and thickening of the lungs with shortness of breath.
- Lung disease.
- A condition that affects the nerves, leading to impairment of sensation, movement and organ function (peripheral neuropathy).

Side effects with unknown frequency; their frequency has not been determined yet:
- Absence of menstruation in women (amenorrhoea).
- Absence of sperm in the seminal fluid in men (azoospermia).

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

Reporting of side effects:
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" that can be found on the home page of the Ministry of Health website (www.health.gov.il) which directs to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il
Additionally, you can report to Padagis via the following address: Padagis.co.il

5. HOW TO STORE THE MEDICINE?

- Avoid poisoning! This medicine, 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 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 package and the bottle label. The expiry date refers to the last day of that month.
- Store in refrigeration (2°C-8°C).
- Can be used for 50 days after first opening, but not later than the expiry date.
- If the doctor instructs you to stop treatment, it is important to return all of the remaining medicine to the pharmacist so he can dispose of it according to the instructions for the disposal of dangerous substances. Keep the remaining medicine with you only according to explicit instruction from the doctor.
- Do not dispose of medicines via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer in use. These measures will help protect the environment.

6. ADDITIONAL INFORMATION

- **In addition to the active ingredient, the medicine also contains:**
  Lactose anhydrous, microcrystalline cellulose, colloidal anhydrous silica, stearic acid, hypromellose, synthetic yellow iron oxide, macrogol/PEG 400, titanium dioxide, synthetic red iron oxide.
- **What the medicine looks like and contents of the package:** Leukeran comes in vials containing 25 brown, round and biconvex coated tablets. Each tablet is engraved with "GX EG3" on one side and "L" on the other side.
- **Registration Holder:** Padagis Israel Agencies Ltd., 1 Rakefet St., Shoham.
- **Manufacturer:** Excella GmbH & Co. KG, Feucht, Germany, for Aspen.
- Revised in April 2023 according to MOH guidelines.
- **Drug registration number in the National Drug Registry of the Ministry of Health:**
  01960.20450

17.04.23