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

The medicine is dispensed with a doctor's prescription only

Myleran Tablets 2 mg

Active ingredient and its quantity:

Each tablet contains: Busulfan 2 mg

Inactive and allergenic ingredients in the preparation - see section 2 "Important information about some of the ingredients in the medicine" and 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 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?

Myleran Tablets 2 mg is intended for supportive therapy for chronic granulocytic leukemia (also called chronic myeloid leukemia).

Therapeutic group: The medicine belongs to a group of antineoplastics and immunomodulators, alkyl sulfonates and cytotoxic medicines (also called chemotherapy).

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are sensitive (allergic) to the active ingredient busulfan or to any of the other ingredients contained in the medicine (see section 6 "Further Information").
- you have been treated with Myleran Tablets in the past and the treatment was unsuccessful.
- you are breast-feeding.

Do not use the medicine if one or more of the aforementioned conditions apply to you.

If you are uncertain, refer to a doctor or pharmacist before taking the medicine.

Special warnings regarding use of the preparation

Before treatment with Myleran Tablets 2 mg, tell the doctor if:

- you are undergoing, or have recently undergone, radiotherapy, or any other chemotherapy, or if you have ever had a stem cell transplant, this is because patients taking Myleran can develop serious liver problems (hepatic veno-occlusive disease). There is an increased risk of developing hepatic veno-occlusive disease if you have had radiotherapy, more than three cycles of chemotherapy or if you have had a stem cell transplant.
- you suffer from an inherited blood problem called thalassemia.
- you have ever had gout (painful and swollen joints caused by accumulation of uric acid crystals). You may need treatment for gout before commencing treatment with Myleran.
- you have a liver, kidney or lung problem.

Busulfan may cause impaired fertility in both males and females. Before starting your treatment you should talk to your doctor. Men who are planning to have children should discuss with the doctor about preserving their sperm before starting treatment.

If you are not sure if any of the sections above apply to you, consult with the doctor or pharmacist before taking the medicine.

Tests and follow-up

During the course of treatment with Myleran, the doctor will perform routine blood tests. This is in order to check your blood cell counts. As a result, the doctor may change the dose.

Drug interactions

If you are taking, or have recently taken, or may take, other medicines, including non-prescription medicines, nutritional supplements and herbal preparations, inform the doctor or pharmacist.

In particular, if you are taking:

- Other cytotoxic drugs (chemotherapy) - when used with Myleran, there is a greater chance of side effects, such as breathing problems.
- Phenytoin (for treating and preventing fits) – the doctor may have to change the phenytoin treatment to a different medicine.
- Vaccines that contain live organisms (such as polio, measles, mumps and rubella) - Myleran can impair your body's capacity to fight infections.
- Itraconazole (for fungal infections) or metronidazole (for bacterial infections) - may cause serious side effects when used with Myleran.
- Cyclophosphamide (to treat certain blood disorders) - if used with Myleran, it is preferable that the first cyclophosphamide dose be given 24 hours or more after the last Myleran dose. This will reduce the chance of any side effects.
- Any anesthetic given in operations in the hospital or at the dentist - in such a case, tell the doctor or dentist that you are taking Myleran.
- Paracetamol - use with caution while taking Myleran.
- Deferasirox (a medicine used to remove excess iron from your body).
- Melphalan (used to treat certain cancers) – in children, it has been reported that treatment with melphalan less than 24 hours after the last Myleran treatment given by mouth may cause more problems (toxicity).

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to become pregnant, consult the doctor or pharmacist before taking the medicine. The doctor will consider the risks and benefits to you and your baby of taking Myleran. This guideline applies to both men and women. Myleran may harm sperm or eggs.

Use a reliable contraceptive method to avoid pregnancy if you or your partner are taking Myleran. Ask your doctor for advice.

If you are pregnant, it is important to consult with a doctor before starting treatment with Myleran.

Do not breast-feed while taking Myleran. Ask your doctor for advice.

Important information about some of the ingredients in the medicine

The medicine contains lactose. If you have been told in the past by your doctor that you have an intolerance to certain sugars, consult the doctor before starting treatment with Myleran Tablets 2 mg.

3. HOW SHOULD YOU USE THE MEDICINE?

Myleran must only be prescribed for you by a doctor specializing in treating blood problems.

Always use the medicine according to the doctor's instructions.

It is important to take the medicine at the appropriate times.

Check with the doctor or pharmacist if you are uncertain about the dose and treatment regimen of the preparation.

The dose and treatment regimen will be determined by the doctor only.

Do not exceed the recommended dose.

Swallow the medicine whole with a glass of water.

Do not break, crush or chew the tablets. The preparation is cytotoxic.

The dose of Myleran:

- The doctor may change the dose during the course of treatment, as necessary.
- The dose can sometimes be changed if you are over-weight.
- If you took an overdose of Myleran, the doctor may prescribe you another medicine from the benzodiazepine group. This medicine will help in preventing fits.

If you accidentally took a higher dose

If you accidentally took a higher dose 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 forgot to take the medicine

If you forgot to take the medicine at the scheduled time, refer to the doctor. **Do not take a double dose to compensate for a forgotten dose.**

If you stop taking the medicine

Adhere to the treatment regimen as recommended by the doctor.

Even if there is an improvement in your health, do not stop the treatment without consulting the doctor.

Do not take medicines in the dark! Check the label and the 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 Myleran Tablets 2 mg 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.

Immediately refer to the specialist or hospital if some of the following symptoms occur:

- any sign of a high fever or infection (sore throat, sore mouth or urinary tract problems).
- any unexpected bleeding or bruising, as these can mean that too few blood cells of a particular type are being produced.
- if you **suddenly** feel unwell (even without a fever).

Additional side effects

Consult with the doctor if any of the following side effects occur:

Very common side effects - effects that occur in more than one user in 10

- a drop in the number of blood cells and platelets.
- feeling sick (nausea), being sick (vomiting), diarrhea, mouth ulcers - with high doses of Myleran.
- yellowing of the whites of the eyes and skin (jaundice) and liver damage - with high doses of Myleran.
- in women: menstruation may stop, fertility may be affected and menopause may start earlier than normal - with high doses of Myleran.
- in girls: the start of puberty may be delayed or may not occur.
- in boys and men: sperm production may be delayed, reduced or stopped, there may be a decrease in testicular size.
- inflammation of the lungs with no signs of infection - called pneumonia syndrome - with high doses of Myleran.

Common side effects - effects that occur in less than one user in 10

- heart rate problems - especially if you have an inherited blood problem called thalassemia.
- inflammation of the lungs which causes breathlessness, cough and fever, called pneumonitis.
- hair loss (with high doses of Myleran).
- appearance of patches of dark skin.
- signs of blood in the urine and pain when passing urine (bladder inflammation) - with high doses of Myleran taken together with a medicine called cyclophosphamide.
- leukemia.

Uncommon side effects - effects that occur in less than one user in 100

- in women: menstruation may stop, fertility may be affected and menopause may start earlier than normal - at usual doses of Myleran.

Rare side effects - effects that occur in less than one user in 1,000

- a severe drop in red blood cell count which can cause tiredness, weakness and bruising and increase your chances of developing infections – a condition called aplastic anemia.
- fits or seizures - with high doses of Myleran.
- cataract or other eye problems - after a bone marrow transplantation and with high doses of Myleran.
- feeling or being sick (nausea or vomiting), diarrhea, mouth ulcers - with usual doses of Myleran. These side effects can be relieved by splitting the dose throughout the day, as per the doctor's instructions.
- jaundice (yellowing of the whites of the eyes and skin) and liver damage - with usual doses of Myleran.
- hair loss (with usual doses of Myleran).
- dry mouth and lips or other skin changes, including very dry skin, itching or rash.

Very rare side effects - effects that occur in less than one user in 10,000

- muscle weakness commonly leading to drooping eyelids and difficulty in speaking or in using the hands and legs – a condition called myasthenia gravis.
- enlargement of breasts in men.
- weakness, increased tiredness, weight loss, feeling sick (nausea), being sick (vomiting) and dark skin patches – which resembles Addison's disease (but with normal activity of the adrenal glands).

Side effects of unknown frequency (effects whose frequency has not yet been determined)

- incomplete development of teeth.

If a side effect occurs, if any of the side effects worsen, or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.

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 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 and bottle. The expiry date refers to the last day of that month.
- Store below 25°C.
- After first opening of the bottle, the medicine can be used for 100 days, 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 in accordance with the guidelines for disposing of hazardous materials. Only keep the remaining medicine if the doctor has explicitly instructed you to do so.

6. FURTHER INFORMATION

- **In addition to the active ingredient, the medicine also contains:**
  Lactose anhydrous, pregelatinised starch, Opadry White (hypromellose, titanium dioxide, triacetin), magnesium stearate.
- **What the medicine looks like and the contents of the package:** Myleran is packaged in a dark glass bottle with a plastic cap, and contains 25 or 100 round and convex white tablets. 'GX EF3' is engraved on one side of each tablet and 'M' on the other side. Not all package sizes may be marketed.
- **Registration holder and its address:** Padagis Israel Agencies Ltd., 1 Rakefet St., Shoham.
- **Name of manufacturer and its address:** Excella GmbH & Co. KG, Feucht, Germany, for Aspen.
- **Registration number of the medicine in the National Drug Registry of the Ministry of Health:** 12938.30943
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