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

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

Puri-Nethol™ Tablets 50 mg

Each tablet contains mercaptopurine 50 mg
Each tablet also contains 59 mg lactose
Additional inactive ingredients - 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 for the treatment of 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?

Puri-Nethol is used to treat different types of leukemia.

Therapeutic group: cytotoxic immunosuppressive drugs.

2. BEFORE USING THE MEDICINE

☒ Do not use the medicine if:
- you are sensitive (allergic) to the active ingredient or to any of the additional ingredients contained in the medicine (see section 6).
- you are breastfeeding.

Special warnings regarding use of this medicine
Avoid contact with the eyes. To prevent irritation, it is important to wash your hands immediately after taking the medicine.

❗ Before treatment with Puri-Nethol, tell the doctor if:
- you are suffering, or have suffered in the past, from impaired function of the liver, kidneys, urinary system.
- you have a known deficiency of the thiopurine methyltransferase (TPMT) enzyme.

❗ If you are taking, or have recently taken, other medicines, including non-prescription medicines, herbal medicines or nutritional supplements, tell the doctor or pharmacist. In particular, inform the doctor or pharmacist if you are taking:
- Methotrexate – to treat cancer.
- Other cytotoxic medicines (chemotherapy) – in combination with Puri-Nethol treatment, these medicines can increase side effects such as breathing problems.
- Allopurinol, oxipurinol and thiopurinol – to treat gout. When these medicines are taken together with Puri-Nethol, take only 25% (one quarter) of the usual Puri-Nethol dosage.
- Anticoagulants (to thin the blood and to prevent formation of blood clots), such as warfarin.
- Olsalazine or mesalazine to treat ulcerative colitis.
- Sulfasalazine to treat rheumatoid arthritis or ulcerative colitis.
- Ribavirin to treat viral infections.

❗ Use of vaccines
If you are due to be vaccinated, inform the doctor that you are taking or have recently taken Puri-Nethol, since vaccines (e.g., polio, measles, mumps and rubella) may cause infections during Puri-Nethol treatment.

❗ Use of the medicine and food
See section 3 "How should you use the medicine?"

❗ Fertility
Do not use Puri-Nethol if you plan to become pregnant and/or plan to have children. This warning applies to both men and women. The medicine can cause damage to the ovaries or sperm. Use reliable contraceptives to prevent pregnancy if you or your partner is taking Puri-Nethol. Refer to the doctor for advice.

❗ Pregnancy and breastfeeding
Treatment with Puri-Nethol is not recommended during pregnancy, especially in the first trimester, as it can cause irreversible damage to the unborn baby. If you become pregnant, think you have become pregnant or plan to become pregnant, consult a doctor before using Puri-Nethol. Do not breastfeed when using Puri-Nethol. Refer to a doctor for advice.

❗ Important information about some of the ingredients in this medicine
Puri-Nethol tablets contain lactose. If the doctor told you that you are sensitive to certain sugars, refer to the doctor before using the medicine.

3. HOW SHOULD YOU USE THE MEDICINE?

Puri-Nethol should only be given to you upon instruction by a doctor specializing in treating blood diseases.
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.
The dosage will be individually determined and depends on the other treatments being given to the patient. It is important to be sure to take the medicine at set intervals.
- Take the medicine at least one hour before or 3 hours after eating food or drinking milk.
- Swallow the medicine whole with a glass of water.
- **The score line on the back of the tablet is not intended for halving the tablet.** It is not recommended to halve, crush or chew the tablets.

Tests and follow-up
During the course of treatment with Puri-Nethol, the doctor will perform routine blood tests. This is to check your blood cell count and liver functions. The doctor may perform other blood and urine tests to monitor uric acid level, which can increase during the course of treatment with Puri-Nethol. The doctor may change the dosage during the course of treatment in accordance with the test results:
- In adult patients – in accordance with kidney and liver function results, the dosage may be reduced.
- In patients with kidney or liver problems – the dosage may be reduced.
- If you have a TPMT enzyme deficiency – the dosage may be reduced.

Do not exceed the recommended dose.

If you accidentally took 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 scheduled time, report to the attending doctor. **Do not take a double dose to compensate for a forgotten dose.**
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.
Do not take medicines in the dark! Check the label and the dose each time you take the 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 Puri-Nethol may cause side effects in some users. Do not be alarmed by the list of side effects. You may not suffer from any of them.

Refer immediately to your specialist doctor or proceed to a hospital if any of the following symptoms occur:
- allergic reactions, such as: rash, high fever, joint pain, facial edema.
- signs of fever or infection (sore throat, mouth ulcers or urinary tract problems). Treatment with Puri-Nethol can cause a drop in the white blood cell count. White blood cells fight infection, and when there are too few of them, infections can occur.
- appearance of **unexpected** bruising or bleeding, as this could indicate inadequate production of certain blood cells.
- if you **suddenly** feel unwell (even without fever).
- yellowing of the skin or whites of the eyes (signs of jaundice)
- if you have severe diarrhea, nausea or vomiting.

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

Very common side effects – occur in more than one in ten users
- a drop in the number of white blood cells and platelets.
- reduced production of bone marrow cells.

Common side effects – occur in 1-10 in 100 users
- nausea or vomiting
- inflammation of the pancreas, which can cause abdominal pains or nausea – in patients with inflammatory bowel disease.
- liver function problems – can be detected by the blood tests.
- yellowing of the skin and/or pain under the ribs or in the area of the stomach (biliary stasis).

Uncommon side effects – occur in 1-10 in 1,000 users
- loss of appetite.
- anemia.

Rare side effects – occur in 1-10 in 10,000 users
- mouth ulcers.
- inflammation of the pancreas which can cause abdominal pains or nausea.
- hair loss.
- acute damage to liver cells (hepatic necrosis).

- allergic reactions together with: rash, persistent fever, joint pain.

Very rare side effects – occur in less than one in 10,000 users

- leukemia.
- lymphoma - in patients with an inflammatory bowel disease when Puri-Nethol is given together with anti-TNF agents.
- ulcers in the intestines.
- in men: reduced sperm count.
- allergic reactions: facial edema.

If a side effect occurs, if one of the side effects worsens 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://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 should be kept in a safe place out of the sight and reach of children and/or infants in order to avoid poisoning. Do not induce vomiting without explicit instruction from the doctor.
- Do not use the medicine after the expiry date (exp. date) that appears on the carton package and bottle label. The expiry date refers to the last day of that month.
- Store in the original package, below 25°C, in a dry place. Protect from light.
- After first opening can be used for 25 days.
- If your doctor tells you to stop the treatment, it is important to return the remains of the medicine to the pharmacist, so he will be able to discard them in accordance with the guidelines for disposal of hazardous materials. Only keep the remaining medicine if your doctor explicitly tells you to do so.

6. FURTHER INFORMATION

- In addition to the active ingredient, the medicine also contains:

  Lactose monohydrate, maize starch, oxidised starch, magnesium stearate, stearic acid.
- What the medicine looks like and the contents of the package: Puri-Nethol is provided in a bottle that contains 25 round, convex, light yellow tablets, with a score line on one side, with GX imprinted above the line and EX2 below the line.
- Registration holder: Perrigo Israel Agencies, Ltd., 29 Lehi Street, Bnei-Brak 51200.
- Manufacturer: Excella GmbH, Feucht, Germany.
- This leaflet was checked and approved by the Ministry of Health in July 2015.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health: 3344.22532