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

Inactive ingredients and allergens in the preparation: see section 2 **"Important information about some of the ingredients of the medicine"** and section 6 in the leaflet **"Further Information"**.

Read the 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 various types of leukemia.

Therapeutic group: Cytotoxic immunosuppressive medicines.

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 ingredients contained in the medicine (see section 6).
- You are breastfeeding.

Special warnings regarding the use of the medicine

Before treatment with Puri-Nethol, tell the doctor if:
- You were recently vaccinated or are about to be vaccinated. When you are taking Puri-Nethol, do not get vaccinated by live attenuated vaccines (such as flu, BCG and measles) until the doctor confirms that this is safe for you, as certain vaccines may cause infections during treatment with Puri-Nethol.
- You suffer from liver dysfunction or liver damage.
- You are aware of a genetic deficiency of the enzyme thiopurine methyltransferase (TPMT).
- You are aware of a sensitivity to a medicine called azathioprine (also used to treat cancer).
- You suffer from a kidney dysfunction.
- Tell the doctor whether you have, or have not, had chickenpox, shingles, or hepatitis B (a liver disease caused by hepatitis B virus).
- You are aware of a genetic disorder called Lesch-Nyhan Syndrome.

If you are receiving treatment to suppress the immune system, taking Puri-Nethol may increase your risk for:
- Tumors, including skin cancer. Therefore, during the treatment with the medicine, avoid prolonged exposure to sunlight, wear protective clothing and use sunscreen with a high protection factor.
- Lymphoproliferative disorders:
  - Treatment with Puri-Nethol increases the risk for a certain type of cancer called lymphoproliferative disorder. When the treatment includes a number of immunosuppressive medicines (including thiopurines), this condition may lead to death.
  - A combination of multiple immunosuppressive medicines, given concomitantly, increases the risk for lymphatic system disorders due to a viral infection [Epstein-Barr virus (EBV) associated lymphoproliferative disorders].

Taking Puri-Nethol may increase your risk for:
- Developing a dangerous condition called macrophage activation syndrome (hyperactivation of white blood cells related to inflammation processes) which usually occurs in people suffering from certain types of arthritis.

Infections

When you are treated with Puri-Nethol, the risk of a viral, fungal or bacterial infection is increased, and the infection may be more serious. See also section 4 **"Side effects"**. Tell your doctor before starting treatment whether or not you have had chickenpox, shingles or hepatitis B.

Children and adolescents

Low blood sugar values (sweating more than usual, nausea, dizziness, confusion etc.) have been reported in a number of children receiving Puri-Nethol, although most of the children were under 6 years of age and had a low body weight.

If you are not sure if this applies to you, consult the doctor or pharmacist before taking Puri-Nethol.

Blood tests (see also section 3 **"How should you use the medicine?"**).

Treatment with Puri-Nethol may affect the bone marrow. This means that you may have a lower number of white blood cells, platelets and red blood cells (less common) than usual. At the beginning of the treatment the doctor will refer you to do a daily blood test, and at least a weekly test during the treatment. This is in order to monitor the levels of these cells in your blood. If you stop the treatment early enough, the blood cell levels will return to normal values.

Additional laboratory tests

The doctor may refer you to do additional tests (urine, blood etc.).

Liver function

Puri-Nethol has a toxic effect on the liver. Therefore, the doctor will refer you to weekly liver function tests during the treatment with Puri-Nethol. If you already have a liver disease or if you are taking additional medicines that have an effect on the liver, the frequency of the tests will increase. If you notice yellowing of the whites of the eyes or of the skin (jaundice), report this to the doctor immediately, as it may be necessary to immediately stop the treatment with Puri-Nethol.

If you are not sure whether the above applies to you, refer to the doctor or pharmacist before taking Puri-Nethol.

Drug interactions

If you are taking, or have recently taken other medicines, including non-prescription medicines, herbal remedies and nutrition supplements, tell the doctor or pharmacist. Especially if you are taking:
- Ribavirin (to treat viral infections).
- Other cytotoxic medicines (chemotherapy to treat cancer).
- Allopurinol, thiopurinol, oxypurinol, or febuxostat (to treat gout).
- Olsalazine (to treat ulcerative colitis).
- Mesalazine (to treat Crohn's disease).
- Sulfasalazine (to treat rheumatoid arthritis or ulcerative colitis).
- Methotrexate (to treat rheumatoid arthritis or severe psoriasis).
- Infliximab (to treat Crohn's disease or ulcerative colitis, rheumatoid arthritis, ankylosing spondylitis or severe psoriasis).
- Warfarin or acenocoumarol – anticoagulants (to thin the blood).

Use of vaccines

If you are due to be vaccinated, consult first with the doctor or nurse. When you are taking Puri-Nethol, do not get vaccinated with live attenuated vaccines (e.g., flu, BCG and measles) until the doctor confirms that this is safe for you, as certain vaccines may cause infections during treatment with Puri-Nethol.

Use of the medicine and food

See section 3 **"How should you use the medicine?"**.

Pregnancy, breastfeeding and fertility

If you have become pregnant, or if you are breastfeeding, think you may have become pregnant or are planning a future pregnancy, consult the doctor before using Puri-Nethol.

Pregnancy

The treatment with Puri-Nethol is not recommended during pregnancy, especially in the first trimester, because it may cause damage to the fetus. If you have become pregnant, your doctor will weigh the risks and benefits for you and your fetus before recommending Puri-Nethol.

Breastfeeding

Do not breastfeed while using Puri-Nethol. Consult the doctor.

Fertility

Use reliable contraceptives in order to prevent pregnancy, if you or your partner are taking Puri-Nethol, for the entire period of the treatment and at least 3 months after taking the last dose. This warning applies to both men and women.

Driving and using machines

It is not expected that Puri-Nethol will affect the ability to drive or use machines, but no studies have been performed to confirm it.

Important information about some of the ingredients of the medicine

Puri-Nethol tablets contain lactose. If the doctor has told you that you have an intolerance 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 on the instruction of a doctor who specializes in treating blood diseases.

Always use the preparation according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only. The dosage will be determined individually and depends on other treatments being given to the patient. It is important to be sure to take the medicine at designated times.
- Take the medicine at least one hour before or 3 hours after food or drinking milk.
- Swallow the medicine whole with a glass of water.
- **The score line on 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 treatment with Puri-Nethol the doctor will perform routine blood tests. This is to check your blood cell count and liver function. The doctor may perform other blood and urine tests to monitor uric acid level, that can rise during treatment with Puri-Nethol. The doctor may change the dosage during treatment in accordance with the test results:
- In adult patients – in accordance with the results of kidney and liver functions 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 have accidentally taken a higher dosage

If you have taken an overdose or if a child or anyone else has accidentally swallowed the medicine, proceed immediately to the 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 designated time, tell the attending doctor. **Do not take a double dose to make up for a forgotten dose.**

If you stop taking the medicine

Adhere to the treatment as recommended by the doctor. Even if there is an improvement in your health, do not stop the 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 a medicine. Wear glasses if you need them.

If you have further questions regarding the 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 when reading the list of side effects. You may not suffer from any of them.

Refer immediately to your specialist doctor or the hospital if any of the following symptoms appears:
- An allergic reaction including swelling of the face or sometimes the mouth and the throat (a very rare effect).
- An allergic reaction including joint pain, rash, high fever (a rare effect).
- Yellowing of the skin or the white of the eye. If this occurs, immediately stop the treatment with Puri-Nethol.
- Signs of fever or infection (sore throat, mouth ulcers or urinary tract problems) or appearance of unexpected bruising or bleeding. Treatment with Puri-Nethol affects the bone marrow and leads to a reduction in the white blood cell and platelet counts (a very common effect).

Consult the doctor if you have one of the following side effects:

Common side effects – appear in 1-10 out of 100 users
- Nausea or vomiting.
- Low red blood cell count (anemia).

Uncommon side effects – appear in 1-10 out of 1,000 users
- Loss of appetite.

Rare side effects – appear in 1-10 out of 10,000 users
- Mouth ulcers.
- Pancreatitis that can cause abdominal pain or nausea.
- Hair loss.
- Damage to liver cells (liver necrosis).
- Various types of cancer including blood, lymph and skin cancer.

Very rare side effects – appear in less than one out of 10,000 users
- Blood cancer (leukemia).
- Spleen and liver cancer [in patients with inflammatory bowel disease (IBD)].
- Intestinal ulcers; symptoms may include abdominal pain and bleeding.
- In men: a decline in the sperm count.

Side effects with unknown frequency (the frequency cannot be quantified from the existing data)
- Increased sensitivity to sunlight and ultra-violet (UV) light.

Additional side effects in children – see in section 2 **"Children and adolescents"**.

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 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" found on the Ministry of Health home page (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

Additionally, you can report to the Company via the following address: Padagis.co.il

5. HOW SHOULD THE MEDICINE BE STORED?
- Avoid poisoning! This medicine, and any other medicine, must be stored in a closed 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 the 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. Keep the bottle tightly closed.
- If your doctor instructs you to stop treatment, it is important to return any tablets which are left to the pharmacist so that he/she can dispose of them according to the guidelines for disposal of dangerous substances. Keep the remainder of the medicine with you, only upon specific instruction of the doctor.

6. FURTHER INFORMATION
- **In addition to the active ingredient, the medicine also contains:**
  Lactose monohydrate, maize starch, modified maize starch, magnesium stearate, stearic acid.
- **What the medicine looks like and contents of the package:**
  Round and convex pale yellow tablets, with a line (which is not used for halving) on one side, where PT is marked above the line and 50 is marked below it, in a glass bottle containing 25 tablets.
- **Registration holder:** Padagis Israel Agencies Ltd., 1 Rakefet St., Shoham.
- **Manufacturer and address:** Aspen Pharma Trading Ltd., Dublin, Ireland.
- Revised in July 2022 according to MOH guidelines.
- Registration number of the medicine in the national medicines registry of the Ministry of Health: 3344.22532