Package Leaflet: Information for the User
Puri-Nethol ® 50 mg tablets
mercaptopurine monohydrate

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor, pharmacist or nurse.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. See section 4

What is in this leaflet

1. What Puri-Nethol is and what it is used for
2. What you need to know before you take Puri-Nethol
3. How to take Puri-Nethol
4. Possible side effects
5. How to store Puri-Nethol
6. Contents of the pack and other information

1. What Puri-Nethol is and what it is used for

Puri-Nethol contains the active substance mercaptopurine monohydrate. Mercaptopurine monohydrate belongs to a group of medicines called cytotoxics (also called chemotherapy) and works by reducing the number of new blood cells your body makes.
Puri-Nethol is used to treat cancer of the blood (leukaemia) in adults, adolescents and children. This is a fast-growing disease which increases the number of new white blood cells. These new white blood cells are immature (not fully formed) and unable to grow and work properly. They therefore cannot fight infections and may cause bleeding. Ask your doctor if you would like more explanation about this disease.

2. What you need to know before you take Puri-Nethol

Do not take Puri-Nethol:
If you are allergic to Puri-Nethol (mercaptopurine monohydrate) or any of the other ingredients of this medicine (see section 6).

Do not get vaccinated with yellow fever vaccine whilst you are taking Puri-Nethol because it may be fatal.

Warnings and precautions
Talk to your doctor or pharmacist or nurse before taking Puri-Nethol if:
- you have been vaccinated with yellow fever vaccine or if you have recently received, or are due to receive, a vaccination (vaccine).
- you take Puri-Nethol, you should not have a live organism vaccine (for example: flu vaccine, measles vaccine, BCG vaccine, etc.) until advised it is safe to do so by your doctor. This is because some vaccines may give you an infection if you receive them while you are taking Puri-Nethol.
- you have kidney or liver problems, as your doctor will need to check that they are working properly.
- you have a condition where your body produces too little of the enzyme called TPMT (thiopurine methyltransferase) as your doctor may need to adjust the dose.
- you are planning to have a baby. This applies to both men and women. Puri-nethol may harm your sperm or eggs (see 'Pregnancy, breast-feeding and fertility' below).
- you have an allergy to a medicine called azathioprine (also used to treat cancer)
- you have, or have not, had chicken pox, shingles or hepatitis B (a liver disease caused by a virus)
- you have a genetic condition called Lesch-Nyhan Syndrome

If you are receiving immunosuppressive therapy, taking Puri-Nethol could put you at greater risk of:
- Tumours, including skin cancer. Therefore, when taking Puri-Nethol, avoid excessive exposure to sunlight, wear protective clothing and use protective sunscreen with a high protection factor.
- lymphoproliferative disorders
  - Treatment with Puri-Nethol increases your risk of getting a type of cancer called lymphoproliferative disorder. With treatment regimen containing multiple immunosuppressants (including thiopurines), this may lead to death.
  - A combination of multiple immunosuppressants, given concomitantly increases the risk of disorders of the lymph system due to a viral infection (Epstein-Barr virus (EBV)-associated lymphoproliferative disorders).

Taking Puri-Nethol could put you at greater risk of:
- developing a serious condition called Macrophage Activation Syndrome (excessive activation of white blood cells associated with inflammation), which usually occurs in people who have certain types of arthritis.
- Some patients with inflammatory bowel disease who have received mercaptopurine monohydrate have developed a rare and aggressive type of cancer called Hepatosplenic T-cell Lymphoma (see section 4, Possible side effects).

The use of Puri-nethol for the treatment of inflammatory bowel disease (IBD) is an unlicensed indication

Blood tests
- Treatment with Puri-Nethol may affect your bone marrow. This means you may have a reduced number of white blood cells, platelets and (less commonly) red blood cells in your blood. Your doctor will carry out blood tests daily when you are at the beginning of your treatment (induction) and at least weekly when you are further along into your treatment (maintenance). This is in order to monitor the levels of these cells in your blood. If you stop treatment early enough, your blood cells will return to normal.

Liver function
- Puri-Nethol is toxic to your liver. Therefore, your doctor will carry out weekly liver function tests when you are taking Puri-Nethol. If you already have liver disease, or if you are taking other medications which may affect your liver, your doctor will carry out more frequent tests. If you notice the whites of your eyes or your skin turn yellow (jaundice) tell your doctor immediately as you may need to stop your treatment immediately.

Vitamin B3 deficiency (Pellagra) Tell your doctor immediately if you have diarrhoea, localised pigmented rash (dermatitis) or deterioration of your memory, reasoning and thinking skills (dementia), as these symptoms may indicate a vitamin B3 deficiency. Your doctor will prescribe vitamin supplements (niacin/nicotinamide) to improve your condition.

Infections
- When you are treated with Puri-Nethol the risk of viral, fungal and bacterial infections is increased and the infections may be more serious. See also section 4.
- Tell your doctor before starting treatment whether or not you have had chickenpox, shingles or hepatitis B (a liver disease caused by a virus). If you think you have an infection, talk to your doctor immediately.

Sun and UV light
- While you are taking Puri-Nethol, you are more sensitive to the sun and UV light. You must make sure you limit your exposure to sunlight and UV light, wear protective clothing and use a sun cream with a high sun protection factor (SPF).

NUDT15-gene mutation
If you have an inherited mutation in the NUDT15-gene (a gene which is involved in the break-down of Puri-Nethol in the body), you have a higher risk of infections and hair loss, and your doctor may in this case give you a lower dose.

Children and adolescents
Low blood sugar (sweating more than usual, nausea, dizziness, confusion, etc.) has sometimes been seen in children, mainly in children under the age of six or with a low body mass index. Talk to your child´s doctor if this happens.

If you are not sure if any of the above applies to you, talk to your doctor or pharmacist before taking Puri-Nethol.

Other medicines and Puri-Nethol
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

In particular, tell your doctor or pharmacist if you are taking any of the following:
- Ribavirin (used to treat viruses)
- Other cytotoxic medicines (chemotherapy – used to treat cancer)
- Allopurinol, thiopurinol, oxipurinol or febuxostat (used to treat gout)
- Olsalazine or mesalazine (used to treat a Crohn's disease and bowel problem called ulcerative colitis)
- Sulfasalazine (used to treat rheumatoid arthritis or ulcerative colitis)
- Methotrexate (used to treat cancer, rheumatoid arthritis or skin disease (severe psoriasis))
- Infliximab (used to treat certain bowel diseases (Crohn's disease and ulcerative colitis), rheumatoid arthritis, ankylosing spondylitis or skin disease (severe psoriasis))
- Warfarin or acenocoumarol (used to 'thin' the blood)
- Anti-epileptic medicines such as phenytoin, carbamazepine. Blood levels of anti-epileptic medicines may need to be monitored and doses adjusted if necessary

Having vaccines while you are taking Puri-Nethol
If you are due to receive a vaccination (vaccine) speak to your doctor or nurse before you do so. If you take Puri-Nethol, you should not have a live vaccines (like polio, measles, mumps and rubella) until advised it is safe to do so by your doctor. This is because some vaccines may give you an infection if you receive them while you are taking Puri-Nethol.

Pregnancy, breastfeeding and fertility
Do not take Puri-Nethol if you are planning to have a baby without first speaking to your doctor for advice. This applies to both men and women. Puri-Nethol may harm your sperm or eggs. Reliable contraception must be used to avoid pregnancy whilst you or your partner are taking Puri-Nethol. Both men and women should continue to use effective contraception for at least 3 months after stopping treatment. If you are already pregnant, you must talk to your doctor before taking Puri-Nethol. Puri-Nethol should not be handled by women who are or planning to be pregnant or breast-feeding. Do not breast-feed while taking Puri-Nethol. Ask your doctor, pharmacist or midwife for advice.

Taking Puri-nethol during pregnancy may cause severe, excessive itching without a rash. You may also experience nausea and loss of appetite at the same time, which may indicate a condition called cholestasis of pregnancy (a disease of the liver during pregnancy). Talk with your doctor immediately, as this condition can cause harm to your unborn child.

Driving and using machines
It is not expected that Puri-Nethol will affect your ability to drive or use machines, but no studies have been done to confirm this.

Puri-Nethol tablets contain lactose
If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Puri-Nethol

Puri-Nethol should only be prescribed to you by a specialist doctor who is experienced in treating cancers of the blood.

- When you take Puri-Nethol, your doctor will take regular blood tests. This is to check the number and type of cells in your blood, and to ensure your liver is working correctly
- Your doctor may also ask for other blood and urine tests to monitor how your kidneys are working and to measure uric acid levels. Uric acid is a natural substance made in your body and levels of uric acid can rise while you are taking Puri-Nethol. High levels of uric acid may damage your kidneys
- Your doctor may sometimes change your dose of Puri-Nethol as a result of these tests.

Always take Puri-Nethol exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. It is important to take your medicine at the right times. The label on your pack will tell you how many tablets to take and how often to take them. If the label does not say or if you are not sure, ask your doctor, nurse or pharmacist.

The usual dose for adults and children is 2.5 mg per kilogram of your body weight each day (or alternatively 50 to 75 mg per m^2 of your body surface area each day). Your doctor will calculate and adjust your dose based on your body weight, results of your blood tests, whether or not you are taking other chemotherapy medicines and your kidney and liver function.

Swallow your tablets whole. Do not chew the tablets. The tablets should not be broken or crushed. If you or your caregiver does handle broken tablets, wash the hands immediately.

Puri-Nethol with food and drink
You can take Puri-Nethol with food or on an empty stomach, but the choice of method should be consistent from day to day. You should take your medicine at least 1 hour before or 2 hours after having milk or dairy products.

It is important to take Puri-Nethol in the evening to make the medicine more effective.

If you take more Puri-Nethol than you should
If you take more Puri-Nethol than you should, you may feel sick, vomit or have diarrhoea. Tell your doctor immediately or go to a hospital immediately straight away. Take the medicine pack with you.

If you forget to take Puri-Nethol
Tell your doctor. Do not take a double dose to make up for a forgotten dose.

If you stop taking Puri-Nethol
Do not stop taking your medicine unless your doctor tells you to or you may get a relapse of your condition.
If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

If you get any of the following, talk to your specialist doctor straight away or go to the hospital immediately:
- Allergic reaction, the signs may include:
  - Skin rashes
  - High temperature
  - Joint pain
  - Swollen face
  - Skin nodules (erythema nodosum) (the frequency is unknown)
- Any signs of fever or infection (sore throat, sore mouth or urinary problems)
- Any unexpected bruising or bleeding, as this could mean that too few blood cells of a particular type are being produced
- If you suddenly feel unwell (even with a normal temperature) and have abdominal pain and sickness, as this could be a sign of an inflamed pancreas
- Any yellowing of the whites of the eyes or skin (jaundice)

Talk to your doctor if you have any of the following side effects, which may also happen with this medicine:

Very common (affects more than 1 in 10 people)
- A drop in the number of white blood cells and platelets (may show up in blood tests)

Common (affects less than up to 1 in 10 people)
- Nausea (you feel sick) or vomiting (being sick)
- Liver damage - this may show up in blood tests
- A drop in red blood cells which may make you tired, weak or breathless (called anaemia)
- Loss of appetite
- Inflammation of the pancreas (pancreatitis) in inflammatory bowel disease patients

Uncommon (affects less than 1 in 100 people)
- Inflammation of the pancreas (pancreatitis)
- Joint pain
- Skin rash
- Fever
- Permanent damage to the liver (hepatic necrosis)
- Bacterial and viral infections, infections associated with neutropenia

Rare (affects less than 1 in 1,000 people)
- Hair loss
- Mouth ulcers
- In men: temporary low sperm count
- Allergic reaction leading to swollen face
- Various types of cancers including blood, lymph and skin cancers
- Inflammation of the pancreas (pancreatitis) in patients with leukaemia (cancer of the blood)

Very rare (affects less than 1 in 10,000 people)
- A different type of leukaemia to that being treated
- Ulcers in the intestines; symptoms may include abdominal pain and bleeding

Not known (frequency cannot be estimated from the available data)
- A rare type of cancer (hepatosplenic T-cell lymphoma, in patients with a condition called Inflammatory Bowel Disease), (see section 2, Warnings and Precautions).
- Increased sensitivity to sunlight and UV light causing skin reactions.
- Decrease in blood sugar levels
- burning or tingling sensation in the mouth or lips (inflammation of the mucosa, stomatitis)
- cracked or swollen lips (cheilitis)
- vitamin B3 deficiency (pellagra) associated with a localised pigmented skin rash, diarrhoea or decrease in memory, reasoning or other thinking skills.
- a decrease in clotting factors.

Additional side effects in children
Low blood sugar levels (sweating more than usual, nausea, dizziness, confusion, etc.) have been reported in some children receiving Puri-Nethol, the frequency is not known; However, most of the children were under the age of six years old and had a low body weight.

Reporting of side effects
If you get any side effects or if the side effects get worse, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via
HPRA Pharmacovigilance, Website: www.hpra.ie;
By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Puri-Nethol
- Keep this medicine out of the sight and reach of children.
- Do not use this medicine after the expiry date, which is stated on the bottle label and the carton after 'Exp'. This is printed as month; year and refers to the last date of the month.
- Do not store your Puri-Nethol tablets above 25°C. Store in the original bottle and in the carton in order to protect from light. Keep the bottle tightly closed in order to protect from moisture.
- If your doctor tells you to stop taking the tablets, it is important to return any which are left over to your pharmacist, who will destroy them according to disposal of dangerous substance guidelines.
  Only keep the tablets if your doctor tells you to.

6. Contents of the pack and other information

What Puri-Nethol contains
The active substance is mercaptopurine monohydrate. Each tablet contains 50 mg of mercaptopurine monohydrate.
The other ingredients are lactose monohydrate, maize starch, modified maize starch, stearic acid and magnesium stearate.

What Puri-Nethol looks like and contents of the pack
Puri-Nethol tablets are round, pale yellow in colour and have a score line on one side. The tablets are marked with 'GX' scoreline 'EX2' or 'PT' scoreline '50' and are plain on the other side. Your Puri-Nethol tablets are in bottles of 25 tablets**.**

Manufacturer:
Excella GmbH or Excella GmbH & Co. KG, Nürnberger Strasse 12, Feucht, Germany or Aspen Bad Oldesloe GmbH, Industriestrasse 32-36, 23843 Bad Oldesloe, Germany

The product is procured from within the EU, repackaged and distributed by the Parallel Product Authorisation Holder:
PCO Manufacturing Ltd., Unit 10, Ashbourne Business Park, Ashbourne, Co. Meath, Ireland.

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