

Package Leaflet: Information for the User
Mercaptopurine 50mg 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 Mercaptopurine is and what it is used for
- 2 What you need to know before you take Mercaptopurine
- 3 How to take Mercaptopurine
- 4 Possible side effects
- 5 How to store Mercaptopurine
- 6 Contents of the pack and other information

1 What Mercaptopurine is and what it is used for

Mercaptopurine tablets contain the active substance called 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. Mercaptopurine 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 Mercaptopurine

Do not take Mercaptopurine:

If you are allergic to Mercaptopurine or any of the other ingredients of this medicine (see section 6). Do not get vaccinated with yellow fever vaccine whilst you are taking 6-mercaptopurine because it may be fatal.

Warnings and precautions

Talk to your doctor or pharmacist or nurse before taking Mercaptopurine if:

- you have recently received, or are due to receive, a vaccination (vaccine). If you have been vaccinated with yellow fever vaccine
- you take Mercaptopurine, 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 Mercaptopurine
- 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. mercaptopurine monohydrate may harm your sperm or eggs (see 'Pregnancy, breast-feeding and fertility' below)
- you have an inherited mutation in the NUDT15-gene (a gene which is involved in the breakdown of Mercaptopurine 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

- 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 Mercaptopurine could put you at greater risk of:

- Tumours, including skin cancer. Therefore, when taking Mercaptopurine, avoid excessive exposure to sunlight, wear protective clothing and use protective sunscreen with a high protection factor
- lymphoproliferative disorders:
 - Treatment with Mercaptopurine 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 Mercaptopurine 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 6-mercaptopurine have developed a rare and aggressive type of cancer called Hepatosplenic T-cell Lymphoma (see section 4, Possible side effects)

The use of mercaptopurine monohydrate for the treatment of inflammatory bowel disease (IBD) is an unlicensed indication

Infections

When you are treated with Mercaptopurine 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).

Blood tests

- Treatment with Mercaptopurine 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

- Mercaptopurine is toxic to your liver. Therefore, your doctor will carry out weekly liver function tests when you are taking Mercaptopurine. 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.

Sun and UV light

While you are taking Mercaptopurine, 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).

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 Mercaptopurine.

Other medicines and Mercaptopurine

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 Mercaptopurine

If you are going to have a vaccination speak to your doctor or nurse before you have it. If you take Mercaptopurine, you should not have a live vaccine (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 have them whilst you are taking Mercaptopurine.

Mercaptopurine with food and drink

You can take Mercaptopurine 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.

Pregnancy, breast-feeding and fertility

Do not take mercaptopurine if you are planning to have a baby without first speaking to your doctor for advice. This applies to both men and women. Mercaptopurine may harm your sperm or eggs. Reliable contraception must be used to avoid pregnancy whilst you or your partner are taking mercaptopurine. 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 mercaptopurine. Mercaptopurine should not be handled by women who are or planning to be pregnant or breast-feeding. Do not breast-feed while taking Mercaptopurine. Ask your doctor, pharmacist or midwife for advice.

Talk to your doctor immediately if you experience intense itching without a rash during your pregnancy. You may also experience nausea, and loss of appetite together with itching, which indicates that you have a condition called cholestasis of pregnancy (condition affecting the liver during pregnancy).

Driving and using machines

It is not expected that Mercaptopurine will affect your ability to drive or use machines, but no studies have been done to confirm this.

Mercaptopurine 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 medicine.

3 How to take Mercaptopurine

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

- When you take Mercaptopurine, 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 Mercaptopurine. High levels of uric acid may damage your kidneys
- Your doctor may sometimes change your dose of Mercaptopurine as a result of these tests

Always take Mercaptopurine 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 m² 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.**

Mercaptopurine with food and drink

You can take Mercaptopurine 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 Mercaptopurine in the evening to make the medicine more effective.

If you take more Mercaptopurine than you should

If you take more Mercaptopurine 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 Mercaptopurine

Tell your doctor. Do not take a double dose to make up for a forgotten dose.

If you stop taking Mercaptopurine

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 side effects, 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
 - 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)
 - skin nodules (erythema nodosum) (the frequency is unknown)

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 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 1 in 100 people)

- Joint pain
- Skin rash
- Fever
- Permanent damage to the liver (hepatic necrosis)
- Bacterial and viral infections, infections associated with neutropenia
- cholestasis of pregnancy, which can cause intense itching, especially on the hands and feet

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 Mercaptopurine, 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, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the Yellow Card Scheme at:

www.mhra.gov.uk/yellowcard

By reporting side effects you can help provide more information on the safety of this medicine.

5 How to store Mercaptopurine

- 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 pack after 'Exp'
- Do not store your Mercaptopurine tablets above 25°C. Keep the bottle tightly closed
- 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 Mercaptopurine contains**

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

What Mercaptopurine looks like and contents of the pack

Mercaptopurine tablets are a pale yellow colour and are marked with 'PT / 50'. Your Mercaptopurine tablets are in bottles of 25 tablets.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation holder:
Aspen Pharma Trading Limited
3016 Lake Drive,
Citywest Business Campus,
Dublin 24,

