

Package leaflet: Information for the patient

Azathioprine Tablets 25 mg

Azathioprine Tablets 50 mg

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 or pharmacist.
- 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 or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

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

1. What Azathioprine is and what it is used for

Azathioprine belongs to a group of medicines called immunosuppressants. Azathioprine helps to reduce or suppress your body's own immune system. Your immune system helps to protect you against infections. However, sometimes it can produce illness and unwanted effects. For example, if you have just had an organ transplant, your immune system will try to reject the new organ. Azathioprine helps to prevent this immune response, and so allows the organ to carry on working. It is therefore used together with other medicines such as corticosteroids to improve the survival of organ transplants.

Azathioprine is also used to treat conditions caused by your immune system over reacting or reacting abnormally. For example:

- rheumatoid arthritis (inflammation and pain in your joints)
- hepatitis (inflamed liver)
- systemic lupus erythematosus (a disease which affects your skin and major organs)
- blood disorders such as thrombocytopenia (reduced numbers of blood cells called platelets). This can affect blood clotting and increase the risk of bleeding or bruising.
- haemolytic anaemia (when you do not have enough red blood cells)
- pemphigus (blisters and sores on your skin)
- dermatomyositis (inflammation of your muscles and skin)
- polyarteritis nodosa (inflammation of your blood vessels)

For these conditions, Azathioprine may be used alone, or in combination with other medicines.

2. What you need to know before you take Azathioprine

Do not take Azathioprine if you

- are allergic to azathioprine, to mercaptopurine (a medicine used to treat leukaemia, a cancer of the white blood cells) or any of the other ingredients of this medicine (listed in section 6).
- are pregnant or intend to become pregnant
- are breast-feeding.

Warnings and precautions

Talk to your doctor or pharmacist before taking this medicine if you:

- know you have a metabolic abnormality called Lesch-Nyhan syndrome. Azathioprine is not recommended if you have this condition.
- know you have a shortage of a liver enzyme called thiopurine methyltransferase (TPMT). TPMT breaks down azathioprine and other medicines.
- have liver or kidney disease. You may have to take a lower dose and your doctor will closely monitor you.
- have ever suffered from chickenpox or shingles.
- if you have had hepatitis B (a liver disease caused by a virus)

NUDT15-gene mutation

If you have an inherited mutation in the NUDT15-gene (a gene which is involved in the break-down of Azathioprine 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.

If you are receiving immunosuppressive therapy, taking Azathioprine could put you at greater risk of:

- tumours, including skin cancer. Therefore, when taking Azathioprine, avoid excessive exposure to sunlight, wear protective clothing and use protective sunscreen with a high protection factor.
- lymphoproliferative disorders
 - treatment with Azathioprine 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 Azathioprine 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.
- 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, severe chickenpox or shingles infection. Therefore, you should avoid contact with anyone suffering from chickenpox or shingles.
- a previous hepatitis B infection becoming active again
- other infections such as PML (Progressive Multifocal Leukoencephalopathy) which is an opportunistic infection

If you experience any signs of infection please contact your doctor (see section 4 “Possible side effects”).

Your doctor will need to monitor you closely throughout your treatment. You should therefore visit your doctor regularly whilst taking Azathioprine so your condition can be checked. You will need to have your blood count checked at least once a week for the first two months of treatment and then monthly.

This product may cause you to experience abnormally coloured urine, such as bright yellow urine. Although bright yellow urine is generally not concerning, you should discuss any change in the colour of your urine – including other discolourations or darkening – with your doctor, as this may indicate kidney or liver problems.

Other medicines and Azathioprine

Tell your doctor if you are taking, have recently taken or might take any other medicines. This is because Azathioprine tablets can affect the way some medicines work. Also some other medicines can affect the way Azathioprine works. In particular tell your doctor if you are taking, or are planning to take:

- ribavirin (used to treat viral infections)
- other immunosuppressants e.g. ciclosporin, methotrexate, tacrolimus
- medicines to treat cancer e.g. doxorubicin
- allopurinol, oxipurinol or thiopurinol or other xanthine oxidase inhibitors, such as febuxostat (for gout or kidney stones)
- cimetidine (for gut or stomach ulcers)
- furosemide ('water tablets')
- penicillamine (for rheumatoid arthritis)
- anticoagulants such as warfarin or acenocoumarol (to 'thin' the blood)
- ACE inhibitors such as captopril (for blood pressure or heart failure)
- indomethacin (an anti-inflammatory)
- Trimethoprim/sulfamethoxazole (an antibiotic)
- infliximab, mesalazine, olsalazine, sulfasalazine or balsalazide (mainly used to treat ulcerative colitis and Crohn's disease)
- Muscle relaxants e.g. tubocurarine or succinylcholine (used during operations) as they may interact with Azathioprine. Before a surgical procedure tell the anesthesiologist that you are taking azathioprine because muscle relaxants such as tubocurarine or succinylcholine (used during anesthesia) may interact with azathioprine

If you are going to have an operation, tell your doctor or the hospital staff as Azathioprine can interact with medicines called muscle relaxants (e.g. succinylcholine or tubocurarine), which you might be given during your operation.

if you have recently received, or are due to receive, a vaccination (vaccine). If you take Azathioprine tablets, 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 Azathioprine tablets

Azathioprine with food and drink

You should take your medicine at least 1 hour before or 2 hours after having milk or dairy products.

Pregnancy, breast-feeding and fertility

If you are pregnant or breast-feeding, think you may be pregnant or are planning to become pregnant, ask your doctor for advice before taking this medicine.

Pregnancy

Do not take Azathioprine if you are pregnant, become pregnant, or suspect you may already be pregnant as the product could harm your baby (see section 2 "Do not take Azathioprine" above). Contact your doctor as soon as possible for advice. Do not take Azathioprine if you are planning to have a baby. This applies to both men and women.

You and your partner must use a reliable method of contraception whilst taking Azathioprine.

Breast-feeding

Small amounts of Azathioprine may pass into the breast milk. It is recommended that women receiving Azathioprine should avoid breastfeeding unless the benefits outweighs the potential risks to the child. Ask your doctor for advice before breastfeeding.

Fertility

The effects of Azathioprine tablets on fertility are not known.

Driving and using machines

Do not drive or operate machinery if you feel dizzy while taking this medicine.

Information on sodium content

This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium free'.

3. How to take Azathioprine

Always take this medicine exactly as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure.

Adults, adolescents and children

Your dose will be adjusted depending on your weight. The recommended doses are:

To prevent organ rejection

The recommended starting dose is up to 5 mg per kg of body weight per day. Your doctor will then assess your response to Azathioprine and choose the best dose for you. This may take weeks or months. After this assessment your dose will usually be between 1 and 4 mg per kg of body weight per day.

Other conditions

The recommended starting dose is between 1 and 3 mg per kg of body weight per day. Your doctor will adjust the dose until it is right for you. Your doctor will prescribe the lowest dose that is effective to treat your condition. If there is no improvement within three months, your doctor may stop giving you this medicine.

Older people or people with kidney or liver disease

If you are elderly or you have kidney or liver disease, you may be started on a lower dose of Azathioprine. Your doctor will monitor your blood and liver function carefully. Your dose may be reduced further if there are any signs that your blood or liver is affected.

Taking Azathioprine

- Swallow the tablets whole with a glass of water. Do not break, chew or crush them.
- The 50 mg tablets have a score line but this is not intended for breaking the tablet.
- If you feel sick after taking your Azathioprine, it should help to take your tablets after meals.

It is important that carers are aware of the need for safe handling of this medicine. If you or your caregiver handle broken tablets, wash your hands immediately. Please consult your doctor or pharmacist for advice.

If you take more Azathioprine than you should

Contact your doctor or nearest hospital emergency department **immediately**. Take the container and any remaining tablets with you. Symptoms of overdose include nausea (feeling sick), vomiting and diarrhoea, lack of white blood cells which may cause frequent infections such as fever, severe chills, sore throat or mouth ulcers, disturbances of your liver function, bruising and bleeding.

If you forget to take Azathioprine

If you forget to take your tablets, take the missed dose as soon as you remember. If it is nearly time for your next dose and if you take only one dose a day, do not double your next dose, carry on as usual and check with your doctor. If you miss a dose, check with your doctor.

If you stop taking Azathioprine

Do not stop taking this medicine without talking to your doctor. You may need to take it indefinitely to help stop transplant rejection.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

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

If any of the following happen stop taking Azathioprine and tell your doctor immediately or go to your nearest hospital emergency department:

- allergic reactions, (these are uncommon side effects which may affect up to 1 in 100 people) the signs may include:
 - general tiredness, dizziness, feeling sick (nausea), being sick (vomiting), diarrhoea or abdominal pain
 - swelling of the eyelids, face or lips
 - redness of the skin, skin nodules or a skin rash (including blisters, itching or peeling skin)
 - pain in the muscles or joints
 - sudden wheeziness, coughing or difficulty breathing

In severe cases these reactions may be life-threatening (this is rare which may affect up to 1 in 10,000 people).

- Skin rashes or redness, which may develop into life-threatening skin reactions including widespread rash with blisters and peeling skin, particularly occurring around the mouth, nose, eyes and genitals (Stevens-Johnson syndrome), extensive peeling of the skin (toxic epidermal necrolysis) (these may be very rare side effects which may affect up to 1 in 10,000 people)
- Reversible pneumonitis (inflammation of your lungs causing breathlessness, cough and fever) (these may be very rare side effects which may affect up to 1 in 10,000 people)
- problems with your blood and bone marrow, signs include weakness, tiredness, paleness, bruising easily, unusual bleeding or infections (these may be very common side effects which may affect more than 1 in 10 people)
- when Azathioprine tablets are used in combination with other immunosuppressives you may get a virus which causes damage to your brain. This may cause headaches, changes in behaviour, impaired speech, worsening of abilities such as memory, attention and decision making (cognitive decline) and may be fatal (condition known as JC virus associated Progressive Multifocal Leukoencephalopathy) (these may be very rare side effects which may affect more than 1 in 10,000 people)

If you get any of the following serious side effects, talk to your doctor or specialist doctor immediately, you may need urgent medical treatment:

- you have a high temperature (fever) or other signs of an infection such as sore throat, sore mouth, urinary problems, or chest infection causing breathlessness and cough (these may be very common side effects which may affect more than 1 in 10 people) • problems with your liver, signs include your skin or the whites of your eyes turn yellow (jaundice) (these may be uncommon side effects which may affect up to 1 in 100 people)
- various types of cancers including blood, lymph and skin cancers (see section 2 Warnings and precautions) (these may be rare side effects which may affect up to 1 in 1000 people).
- *Sweet's syndrome* (also known as acute febrile neutrophilic dermatosis). You may develop a rash (raised red, pink or purple lumps which are sore to touch), particularly on your arms, hands, fingers, face and neck, which may also be accompanied by a fever (high temperature) (the rate at which these side effects occur is not known – cannot be estimated from available data)
- a certain type of lymphomas (hepatosplenic T-cell lymphoma). You may develop nose bleeds, fatigue, significant night sweats, weight loss and unexplained fevers (high temperature) (the rate at which these side effects occur is not known – cannot be estimated from available data)

If you notice any of the above, stop taking Azathioprine Tablets and see a doctor straight away.

Other side effects include:

Very common (may affect more than 1 in 10 people):

- low white blood cell level in your blood tests, which may cause an infection

Common (may affect up to 1 in 10 people):

- nausea (feeling sick)

Uncommon (may affect up to 1 in 100 people):

- anaemia (low red blood cell level)
- pancreatitis (inflammation of the pancreas), which may cause severe upper stomach pain

Rare (may affect up to 1 in 1,000 people):

- You might notice some hair loss while taking Azathioprine Tablets. Often hair does grow again, even if you carry on taking Azathioprine Tablets. If you are worried, ask your doctor

Very rare (may affect up to 1 in 1,000 people):

- problems with your bowels leading to diarrhoea, abdominal pain, constipation, feeling or being sick (bowel perforation)

Not known (frequency cannot be estimated from the available data)

- photosensitivity (sensitivity to light or sunlight)

Stop taking Azathioprine and tell your doctor immediately if you come into contact with anyone who is suffering from chickenpox or shingles.

Reporting of side effects

If you get any side effects, 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 the Yellow Card Scheme at: www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Azathioprine

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 carton after EXP. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Azathioprine contains

The active substance is azathioprine. Each tablet contains either 25 mg or 50 mg azathioprine.

The other ingredients are maize starch, microcrystalline cellulose, mannitol, povidone K25, croscarmellose sodium and stearyl fumarate sodium. The film-coating contains hypromellose and macrogol.

What Azathioprine looks like and contents of the pack

Your medicine comes as a pale yellow, round, film-coated tablet.

The 25 mg tablet is marked 'AE' over '25' on one side with a 'G' on the other.

The 50 mg tablet is marked 'AE' over '50' on one side and a scoreline on the reverse.

Azathioprine is available in blister packs or plastic containers of 28, 30, 50, 56, 60, 84, 90, 100, 112, 168, 500 and 1,000 tablets. Not all pack sizes may be marketed.

Marketing Authorisation Holder

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