

PACKAGE LEAFLET: INFORMATION FOR THE USER
Azathioprine 50mg Tablets

Azathioprine

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 50mg Tablets are and what it is used for
2. What you need to know before you take Azathioprine 50mg Tablets
3. How to take Azathioprine 50mg Tablets
4. Possible side effects
5. How to store Azathioprine 50mg Tablets
6. Contents of the pack and other information

1. WHAT AZATHIOPRINE 50MG TABLETS ARE AND WHAT THEY ARE USED FOR

Azathioprine 50mg Tablets contains the active substance azathioprine which belongs to a group of medicines called immunosuppressants. This means that they reduce the strength of your immune system.

Immunosuppressant medicines are sometimes necessary to help your body accept an organ transplant, or to treat some diseases where your immune system is reacting against your own body (autoimmune diseases).

Azathioprine 50mg Tablets are used to:

- Help your body accept a kidney, liver, heart, lung or pancreas transplant. [Azathioprine Tablets are usually used together with other medicines in order to enhance their effect].
- Treat severe rheumatoid arthritis
- Treat severe inflammation of the gut (Crohn's disease or ulcerative colitis)
- Treat some diseases where your immune system is reacting against your own body (autoimmune diseases) including severe inflammatory diseases of the skin, liver, arteries and some blood disorders.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE AZATHIOPRINE 50MG TABLETS

Do not take Azathioprine 50mg Tablets:

- If you are allergic to azathioprine, 6-mercaptopurine or any of the other ingredients of this medicine (listed in section 6)
- If you have a severe infection
- If you have severe liver disease or severe bone marrow disease
- If you have an inflamed pancreas
- If you need or are going to have a vaccination containing a living virus or bacteria, such as BCG, smallpox or yellow fever vaccine
- If you are pregnant, unless your doctor thinks it is absolutely necessary (see "Pregnancy, breast-feeding and fertility")
- If you are breast-feeding (see "Pregnancy, breast-feeding and fertility")

Warnings and precautions

Talk to your doctor or pharmacist before taking Azathioprine 50mg Tablets:

- If you have or have ever had any liver or kidney problems
- If you have a condition where your body produces too little of a natural chemical called thiopurine methyltransferase (TPMT)
- If you have an infection for which you have not yet received treatment
- If you are pregnant or trying to become pregnant (see "Pregnancy, breast-feeding and fertility")
- If you are going to have an operation (this is because medicines including tubocurarine, pancuronium or succinylcholine used as muscle relaxants during operations may interact with Azathioprine 50mg Tablets)
- If you have a rare genetic disorder called "Lesch-Nyhan syndrome".
- If you are receiving immunosuppressive therapy, taking Azathioprine 50mg Tablets could put you at greater risk of:
 - tumours, including skin cancer. Therefore, when taking Azathioprine 50mg Tablets, avoid excessive exposure to sunlight, wear protective clothing and use protective sunscreen with a high protection factor.
 - lymphoproliferative disorders
 - treatment with Azathioprine 50mg Tablets 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 viral infection (Epstein-Barr virus (EBV)-associated lymphoproliferative disorders).

Taking Azathioprine 50mg Tablets 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.

You should take care to avoid too much sun (including sunbeds) whilst taking Azathioprine Tablets.

You must use contraceptive methods whilst taking these tablets and for up to 3 months after you have finished taking them. Suitable methods of contraception should be discussed with your doctor. Women using intra uterine devices (IUDs) should use additional contraceptive methods while taking Azathioprine Tablets.

NUDT15-gene mutation

If you have an inherited mutation in the NUDT15-gene (a gene which is involved in the breakdown of Azathioprine 50mg Tablets 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.

Other medicines and Azathioprine 50mg Tablets

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. The following medicines may interact with Azathioprine Tablets:

- Allopurinol, oxipurinol or thiopurinol (used mainly to treat gout)
- Ciclosporin or tacrolimus (also used as immunosuppressant medicines)
- Infliximab (used to treat inflammation of the bowels [Crohn's disease])
- Olsalazine, mesalazine or sulfasalazine (used mainly to treat ulcers or chronic inflammation of the colon and anal passage)
- Warfarin or phenprocoumon (used to prevent blood clots)
- ACE-inhibitors (used to treat high blood pressure and heart failure)
- Furosemide (used mainly to treat high blood pressure)
- Trimethoprim/sulfamethoxazole (used to treat bacterial infections)
- Cimetidine (used to treat stomach ulcers and indigestion)
- Indometacin (used as a painkiller and to treat inflammation)
- Cytotoxic medicines - also called "chemotherapy" (used to treat cancer)
- Vaccines (such as hepatitis B vaccine)
- Curare, d-tubocurarine, pancuronium or succinylcholine (used as muscle relaxants during operations). You should inform your anaesthesiologist of your treatment with Azathioprine 50mg Tablets prior to surgery.

Pregnancy, breast-feeding and fertility

Azathioprine 50mg Tablets should only be taken if your doctor thinks it is absolutely necessary. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Women of childbearing potential and men must use effective contraception during treatment with Azathioprine and for at least 3 months after the treatment is discontinued. Azathioprine has been reported to interfere with the effectiveness of intrauterine contraceptive devices (IUCD) therefore additional contraceptive measures are recommended.

Do not take the tablets if you are breast-feeding.

Driving and using machines

Studies on the effects of azathioprine on the ability to drive and use machines have not been performed. This product may cause dizziness, which could affect a patient's ability to drive.

3. HOW TO TAKE AZATHIOPRINE 50MG TABLETS

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

The label on the carton will tell you how many tablets to take and when. The tablets should be swallowed whole with one full glass of water (about 200ml). Take your tablets during meals.

Your doctor will monitor how you respond to your medicine and may change your dose if required.

Whilst you are taking Azathioprine 50mg Tablets your doctor will want you to have a complete blood test performed, at least once a week, during the first 8 weeks of treatment. In certain situations, your doctor may decide to carry out blood tests more frequently.

After 8 weeks the frequency of the testing may be reduced and your doctor may ask you to repeat the complete blood test every month or at least at intervals of no longer than 3 months.

After organ transplant

A dose of 5mg per kilogram of your bodyweight per day may be given on the 1st day of your treatment. However, the usual maintenance dose is between 1 and 4mg per kilogram of your bodyweight per day. Your doctor may adjust this dose according to your body's response to your medicine.

Patients with chronic active hepatitis

The usual dose is between 1 and 1.5mg per kilogram of your bodyweight per day.

Other conditions

The usual starting dose is between 1 and 3mg per kilogram of your bodyweight per day. Your doctor will adjust the dose until it is right for you.

Use in children and adolescents

Where treatment is recommended, the dosage for children and adolescents is the same as the adult dose.

Elderly patients or patients with kidney or liver disease

A smaller adult dose may be required.

If you have taken more Azathioprine 50mg Tablets than you should

In the event of overdose the most likely effect is bone marrow suppression reaching its maximum 9-19 days after dosing. You may get a sore throat, fever or infection. You may also feel tired or experience bruising and bleeding. If you have taken too many tablets, contact your doctor or go to the nearest hospital casualty department immediately. Remember to take the pack and any remaining tablets with you to show the doctor.

If you forget to take your Azathioprine 50mg Tablets

Do not take a double dose to make up for a forgotten tablet. Wait and take your next dose at the usual time. If you have missed more than one dose, contact your doctor for advice.

If you stop taking Azathioprine 50mg Tablets

Do not stop taking your medicine unless the doctor tells you because stopping your medicine can make your condition worse.

If your doctor does not see an improvement in your condition within three to six months, your doctor may wish to gradually reduce your dose and finally stop giving you this medicine.

It is important that you stop your treatment gradually. You should stop taking the tablets slowly, over a period of time.

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.

You should tell your doctor immediately if you:

- **Get any ulcers in the throat, fever, bruises or bleeding, or you think you have an infection.**
- **Experience any sudden wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting the whole body).**

The following side effects have been reported. Tell your doctor if any of these side effects become troublesome:

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

- Infections (in kidney transplant patients)
- Reduction in number of white blood cells which makes infections more likely
- Feeling and being sick (nausea and vomiting)
- Loss of appetite (anorexia).

Common side effects (may affect up to 1 in 10 people)

- Increased infections in patients with bowel inflammation
- Reduction in blood platelets which increases risk of bleeding or bruising
- Decrease in red blood cells in the blood (anaemia)
- Decrease in white blood cells in patients with rheumatoid arthritis
- Liver disease
- Certain types of cancer (lymphomas, cancer of the cervix, vulva and skin (especially on areas of the skin exposed to the sun)) are common in patients after kidney transplant
- Inflammation of the pancreas, which causes severe pain in the abdomen and back

Uncommon side effects (may affect up to 1 in 100 people)

- Increased infections in patients suffering from rheumatoid arthritis
- Blood disorder after transplant surgery
- Foul smelling stools which are bulky, loose and greasy
- Allergic reactions including dizziness or feeling unwell, low number of white blood cells, low blood pressure, fever, feeling cold, feeling severely sick and vomiting, diarrhoea, rash, rigors, kidney problems, muscle pain (myalgia), pain in the joint (arthralgia), inflammation of blood vessels (vasculitis), high number of liver enzymes
- Hair loss (alopecia)
- Liver problems in patients with rheumatoid arthritis

Rare side effects (may affect up to 1 in 1000 people)

- Paleness, fatigue or shortness of breath caused when the body's bone marrow is not producing enough blood cells (aplastic anaemia)
- Cough and fever caused by pneumonia or inflammation of the lung
- Following transplantation, stomach ulcers (which can bleed) and disease which may cause heartburn, vomiting, general discomfort in the stomach
- Following transplantation, bowel problems leading to diarrhoea, abdominal pain and constipation
- Blood and bone marrow disorders (including granulocytopenia, pancytopenia, megaloblastic anaemia, erythroid hypoplasia and agranulocytosis)
- Severe liver damage which can be life threatening
- Sensitivity to sunlight which can cause skin discolouration or a rash
- Various types of cancers including blood, lymph and skin cancers.

Very rare side effects (may affect up to 1 in 10,000 people)

- Blood disorders (including acute myeloid leukaemia and myelo-dysplastic syndromes)
- Severe allergic reaction which can be life-threatening
- Severe skin conditions (Stevens-Johnson syndrome and toxic epidermal necrolysis) which can be life threatening.

Not known (cannot be estimated from the available data)

- Sudden onset skin condition, which usually affects the head, neck, arms and legs, known as 'Sweet's syndrome' (or acute febrile neutrophilic dermatosis).

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

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

5. HOW TO STORE AZATHIOPRINE 50MG TABLETS

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.

Store in the original package in order to protect from light.

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 50mg Tablets contain

The active substance is azathioprine. Each tablet contains 50mg of azathioprine.

The other ingredients are:

Tablet core: Microcrystalline cellulose, Mannitol, Maize starch, Povidone K25, Croscarmellose sodium, Sodium stearyl fumarate.

Tablet coat: Hypromellose, Macrogol 400.

What Azathioprine 50mg Tablets look like and contents of the pack

Azathioprine 50mg Tablets are light yellow, round, biconvex tablets, engraved with "AZA" and "50" separated by a line on one side and plain on the other side.

Azathioprine 50mg Tablets are available in blister packs containing 50, 56 and 100 tablets.

Not all pack sizes may be marketed.

Marketing Authorisation Holder

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