Package leaflet: Information for the patient

Azathioprin Actavis 50 mg film-coated 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 Azathioprin Actavis is and what it is used for

Azathioprin Actavis contains the active substance azathioprine. It belongs to a group of medicines called immunosuppressives. This means that they reduce the strength of your immune system.
Azathioprin Actavis may be used to help your body accept an organ transplant, such as a new kidney, heart or liver, or to treat some diseases where your immune system is reacting against your own body (autoimmune diseases).

Autoimmune diseases may include
- severe rheumatoid arthritis (a disease where the immune system attacks cells lining the joints causing swelling, pain, stiffness of the joints),
- systemic lupus erythematosus (a disease where the immune system attacks many of the body's organs and tissues, including skin, joints, kidneys, brain, and other organs causing severe fatigue, fever, stiffness and joint pain),
- dermatomyositis and polymyositis (a group of diseases causing inflammation of the muscles, muscle weakness and skin rash),
- auto-immune chronic active hepatitis (a disease in which the immune system attacks liver cells causing liver inflammation, fatigue, muscle aches, yellowing of the skin and fever),
- pemphigus vulgaris (a disease in which the immune system attacks skin cells causing severe blistering of the skin, mouth, nose, throat and genitals),
- polyarteritis nodosa (a rare disease that causes inflammation of the blood vessels),
- auto-immune haemolytic anaemia (a serious blood disorder where the body destroys red blood cells quicker than it can produce them, with symptoms of weakness and shortness of breath),
- chronic refractory idiopathic thrombocytopenic purpura (a condition with low platelet counts, that can cause easy or excessive bruising and bleeding).

Azathioprin Actavis may also be used to treat inflammatory bowel disease (Crohn's disease or ulcerative colitis).

Your doctor has chosen this medicine to suit you and your condition.

Azathioprin Actavis may be used on its own, but it is more often used in combination with other medicines.

Azathioprine which is contained in Azathioprin Actavis may also be authorised to treat other conditions which are not mentioned in this leaflet. Ask your doctor or pharmacist if you have further questions.

2. What you need to know before you take Azathioprin Actavis

Do not take Azathioprin Actavis
- if you are allergic to azathioprine or any of the other ingredients of this medicine (listed in section 6).
- if you are allergic to mercaptopurine (a medicine which is similar to azathioprine).

Warnings and precautions
Talk to your doctor or pharmacist before taking Azathioprin Actavis
- if you have recently received, or are due to receive, a vaccination (vaccine). If you take Azathioprin Actavis, you should not have a live organism vaccine (e.g., 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 Azathioprin Actavis.
- if you have a genetic condition known as Lesch-Nyhan Syndrome. This is a rare condition that runs in families caused by a lack of something called HPRT or 'hypoxanthine-guanine-phosphoribosyltransferase'.
- if you have liver or kidney problems.
- if you have a genetic condition called TPMT deficiency (where your body produces too little of an enzyme called thiopurine methyltransferase).
- if you have ever had chickenpox or shingles.
- if you have had hepatitis B (a liver disease caused by a virus).
- if you are going to have an operation (this is because medicines including tubocurarine, or succinylcholine used as muscle relaxants during operations may interact with azathioprine. You should inform your anaesthesiologist of your treatment with Azathioprin Actavis prior to surgery.

<u>NUDT15-gene mutation</u>
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.

<u>Liver damage</u>
Treatment with Azathioprin Actavis may affect the liver and your doctor will monitor your liver function regularly. Tell your doctor if you experience symptoms of liver damage (see section 4. "Possible side effects").

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

Your doctor will want to take **regular blood samples** while you are taking Azathioprin Actavis, to check for any changes (see section 3. "How to take Azathioprin Actavis"). The frequency of your blood tests will usually decrease the longer you continue to take Azathioprin Actavis.

If you are receiving immunosuppressive therapy, taking Azathioprin Actavis could put you at greater risk of
- tumours, including skin cancer. Therefore, when taking Azathioprin Actavis, avoid excessive exposure to sunlight, wear protective clothing and use protective sunscreen with a high protection factor.
- lymphoproliferative disorders
  - treatment with Azathioprin Actavis 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).

- 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, when taking Azathioprin Actavis, avoid contact with people who have 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").

Vitamin B_3 deficiency (pellagra)
Talk to your doctor immediately if you experience diarrhoea, localised pigmented rash, decline in your memory, reasoning or other thinking skills as these symptoms may suggest vitamin B_3 deficiency (nicotinic acid deficiency/pellagra).

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

- ribavirin (used to treat viral infections)
- methotrexate (mainly used to treat cancers)
- allopurinol, oxipurinol, thiopurinol or other xanthine oxidase inhibitors, such as febuxostat (mainly used to treat gout)
- penicillamine (mainly used in the treatment of rheumatoid arthritis)
- ACE inhibitor (mainly used to treat high blood pressure - hypertension)
- anticoagulants such as warfarin or acenocoumarol (used to prevent blood clots)
- cimetidine (used to treat stomach ulcers and indigestion)
- indomethacin (used as a pain killer and anti-inflammatory)
- cytostatic drugs (drugs used to treat various types of cancer)
- aminosalicylates e.g. olsalazine, mesalazine or sulfasalazine (mainly used in the treatment of ulcerative colitis and Crohn's disease)
- co-trimoxazole (an antibiotic, used to treat infections caused by bacteria)
- infliximab (mainly used in the treatment of ulcerative colitis and Crohn's disease)
- muscle relaxants e.g. tubocurarine or succinylcholine (used during operations) as they may interact with Azathioprin Actavis. Before a surgical procedure tell the anaesthesiologist that you are taking azathioprine because muscle relaxants used during anaesthesia may interact with azathioprine.

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

Having vaccines while you are taking Azathioprin Actavis
If you are due to receive a vaccination (vaccine) speak to your doctor or nurse before you do so. If you take Azathioprin Actavis, you should not have a live vaccine (e.g., 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 Azathioprin Actavis.

Azathioprin Actavis 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
Reliable contraceptive precautions must be taken to avoid pregnancy whilst you or your partner is using Azathioprin Actavis.
If you are pregnant your doctor will carefully consider whether you should take this medicine, based on the risks and benefits of treatment.

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). This condition can cause harm to your unborn child.

Breast-feeding
Small amounts of azathioprine may pass into the breast milk. It is recommended that women receiving Azathioprin Actavis 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 on fertility are not known.

Driving and using machines
Azathioprin Actavis are not known to affect your ability to drive or use machinery. If you experience any side effect from this medicine, you may not be able to drive or operate machinery.

Azathioprin Actavis contains sodium
This medicine contains less than 1 mmol sodium (23 mg) per film-coated tablet, that is to say essentially ‘sodium-free’.

3. How to take Azathioprin Actavis

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 quantity of tablets taken may vary from patient to patient and will be prescribed by your doctor. The dose depends on the condition for which you are being treated.

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

The recommended dose is

Adults

Adults who have had an organ transplant
On the first day of treatment, the usual dose is up to 5 mg per kilogram of body weight, then a usual daily dose of 1-4 mg per kilogram of body weight. During treatment your doctor will adjust the dose depending on your reaction to the medicine.

Adults with other conditions

The usual starting dose is 1-3 mg per kilogram of body weight, then a usual daily dose of less than 1-3 mg per kilogram of body weight During treatment your doctor will adjust the dose depending on your reaction to the medicine.

Elderly patients may need a reduced dose.

Patients with kidney or liver problems may need a reduced dose.

Use in children

Children who have had organ transplant
The dosing for children who have had an organ transplant is the same as adults.

Children with other conditions
The dosing for children with other conditions is the same as adults.
Children who are considered overweight may require a higher dose.

Method of administration
You can take the tablets with food or on an empty stomach but the choice of method should be consistent from day to day. Some patients feel nausea (sick) when first given Azathioprin Actavis, this may be relieved by taking the tablets after food.
Swallow your tablets whole with a large glass of water. Do not chew the tablets. The tablets should also not be broken or crushed.

If you take more Azathioprin Actavis than you should
If you take too many tablets, contact your doctor or pharmacist **immediately**.

If you forget to take Azathioprin Actavis
Do not take a double dose to make up for the dose that you missed. Inform your doctor if you do miss a dose. If it is almost time for your next dose, skip the dose you missed and take your next dose when you are meant to. Otherwise, take it as soon as you remember, then go back to taking it as you would normally.

If you stop taking Azathioprin Actavis
Before you stop taking the tablets, consult with your doctor or pharmacist. Do not stop taking the tablets until your doctor tells you it is safe to do so.

If you have 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.

Stop taking Azathioprin Actavis and see a doctor straight away, if you notice any of the following serious side effects, you may need urgent medical treatment

- 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
  - chest pain, shortness of breath or swollen legs (heart problems)

  In severe cases these reactions may be life-threatening (this is very 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 Azathioprin Actavis is 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 up to 1 in 10,000 people).
- reversible swelling of the brain with symptoms including severe headache, vision changes, seizures, confusion and reduced consciousness, with or without high blood pressure (Posterior Reversible Encephalopathy Syndrome or PRES).

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).
- severe liver damage which can be life threatening, especially in patients who receive long-term treatment (like liver injury, non-cirrhotic portal hypertension, portosinusoidal vascular disease). Tell your doctor if you experience any of the following symptoms: yellowing of the skin and the whites of the eyes (jaundice), bruising easily, abdominal discomfort, loss of appetite, fatigue, nausea, or vomiting (the rate at which these side effects occur is not known - cannot be estimated from available data.)
- 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 (Sweet’s syndrome, also known as acute febrile neutrophilic dermatosis). 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).

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)
- cholestasis of pregnancy, which can cause intense itching, especially on the hands and feet
- 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 Azathioprin Actavis. Often hair does grow again, even if you carry on taking Azathioprin Actavis. If you are worried ask your doctor.

Very rare (may affect up to 1 in 10,000 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)
- vitamin B_3 deficiency (pellagra) associated with a localised pigmented skin rash, diarrhoea and decrease in memory, reasoning or other thinking skills
- inflammation of a salivary gland (sialoadenitis)
- tremor

Reporting of side effects
If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Azathioprin Actavis

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 Azathioprin Actavis contains

The active substance is azathioprine.
Each film-coated tablet contains 50 mg azathioprine.

The other ingredients are: microcrystalline cellulose, mannitol, maize starch, povidone, crosscarmellose sodium, sodium stearyl fumarate, hypromellose and macrogol 400.

What Azathioprin Actavis looks like and contents of the pack

The tablets are light yellow, circular, biconvex, film-coated and engraved with ”AZA” and ”50”, separated by a line on one side and plain on the other side.
The score line is not intended for breaking the tablet.

Pack sizes: 14, 20, 28, 30, 50, 56, 98, and 100 film-coated tablets in blister packs.
Not all pack sizes may be marketed.

Marketing Authorisation Holder

[To be completed nationally]

Manufacturers

[To be completed nationally]

This leaflet was last revised in 18 Dec 2025