Package leaflet: Information for the patient

Azathioprine 25 mg, filmomhulde tablet
Azathioprine 50 mg, filmomhulde tablet

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 [Nationally approved name] are and what they are used for

[Nationally approved name] contain the active substance azathioprine. They belong to a group of medicines called immunosuppressives. This means that they reduce the strength of your immune system.

[Nationally approved name] 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).

[Nationally approved name] 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.

[Nationally approved name] may be used on its own, but it is more often used in combination with other medicines.

2. What you need to know before you take [Nationally approved name]

Do not take [Nationally approved name]:

- 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 the active substance contained in [Nationally approved name].

Warnings and precautions

Talk to your doctor or pharmacist before taking [Nationally approved name]:

- if you have recently received, or are due to receive,a vaccination (vaccine). If you take [Nationally approved name], 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 [Nationally approved name]
- 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 [Nationally approved name]. You should inform your anaesthesiologist of your treatment with [Nationally approved name] prior to surgery.

If you are not sure if any of the above apply to you, talk to your doctor, nurse or pharmacist before taking this medicine.

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

If you are receiving immunosuppressive therapy, taking [Nationally approved name] could put you at greater risk of:

- tumours, including skin cancer. Therefore, when taking [Nationally approved name], avoid excessive exposure to sunlight, wear protective clothing and use protective sunscreen with a high protection factor.
- Lymphoproliferative disorders
    - treatment with [Nationally approved name] 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 [Nationally approved name], 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").

Infections
When you are treated with azathioprine 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).

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.
Other medicines and [Nationally approved name]

Tell your doctor if you are taking, have recently taken or might take any other medicines.. This is because this medicine can affect the way some medicines work. Also some other medicines can affect the way this medicine 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 [Nationally approved name]. Before a surgical procedure tell the anesthesiologist that you are taking azathioprine because muscle relaxants used during anesthesia may interact with [Nationally approved name].

If you are not sure if any of the above apply to you, talk to your doctor or pharmacist before taking [Nationally approved name].

Having vaccines while you are taking [Nationally approved name]
If you are due to receive a vaccination (vaccine) speak to your doctor or nurse before you do so. If you take [Nationally approved name], you should not have a live 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 [Nationally approved name]

[Nationally approved name] 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 (see section 2 "Warnings and precautions").

Pregnancy
Reliable contraceptive precautions must be taken to avoid pregnancy whilst you or your partner is taking [Nationally approved name].
If you are pregnant your doctor will carefully consider whether you should take this medicine, based on the risks and benefits of treatment.

Breast-feeding
Small amounts of [Nationally approved name] may pass into the breast milk. It is recommended that women receiving [Nationally approved name] should avoid breastfeeding unless the benefits outweighs the potential risks to the child. Ask your doctor for advice before breastfeeding.

Fertility
The effects of [Nationally approved name] on fertility are not known.

Driving and using machines

[Nationally approved name] 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.

[Nationally approved name] contain lactose

[Nationally approved name] contain lactose monohydrate. If you have been told by your doctor that you have intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take [Nationally approved name]

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 [Nationally approved name] 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.

You can take [Nationally approved name] 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 [Nationally approved name], this may be relieved by taking the tablets after food.

- When you take [Nationally approved name], 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 [Nationally approved name]. High levels of uric acid may damage your kidneys

Your doctor may sometimes change your dose of [Nationally approved name] as a result of these tests.

Azathioprine 25 mg
Swallow your tablets whole. Do not chew the tablets. The tablets should not be broken or crushed.

Azathioprine 50 mg
The score line is only there to help you break the tablet if you have difficulty swallowing it whole.

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

The recommended dose is:

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 to 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 mg to 3 mg per kilogram of body weight, then a usual daily dose of less than 1 mg to 3 mg per kilogram of body weigh. 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.

If you take more [Nationally approved name] than you should

If you take too many tablets, contact your doctor or pharmacist **immediately**.

If you forget to take [Nationally approved name]

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 [Nationally approved name]

Before you stop taking [Nationally approved name], consult with your doctor or pharmacist. Do not stop taking [Nationally approved name] until your doctor tells you it is safe to do so.

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

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them. The following side effects may happen with this medicine:

Stop taking this medicine 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

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 {(Invented) name strength pharmaceutical form 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 more than 1 in 10,000 people)

If you get any of the following 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).
- 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)

If you notice any of the above, stop taking [Nationally approved name] 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 you severe upper stomach pain,

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

- You might notice some hair loss while taking [Nationally approved name]. Often hair does grow again, even if you carry on taking [Nationally approved name]. 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)

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 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 **[nationally completed name]**

Keep this medicine out of the sight and reach of children.

This medicinal product does not require any special storage conditions.

Do not use this medicine after the expiry date which is stated on the blister strip and on the carton after "EXP". The expiry date refers to the last day of that month.

If the Azathioprine 50 mg film-coated tablet has to be halved, contact of the skin with the powder or the broken part of the tablet should be avoided.
Residues should be disposed of with the same caution.

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

6. Contents of the pack and other information

What [nationally completed name] contains

- The active substance is azathioprine.
  Each film-coated tablet contains 25 mg azathioprine.
- The other ingredients are lactose monohydrate, maize starch, povidone K25, colloidal silicon dioxide, magnesium stearate, hypromellose, microcrystalline cellulose, macrogol stearate 400, talc. Colouring agent: titanium dioxide (E171).

- The active substance is azathioprine.
  Each film-coated tablet contains 50 mg azathioprine.
- The other ingredients are lactose monohydrate, maize starch, povidone K25, colloidal silicon dioxide, magnesium stearate, hypromellose, microcrystalline cellulose, macrogol stearate 400, talc. Colouring agent: titanium dioxide (E171).

What [nationally completed name] looks like and contents of the pack

[Nationally completed name] film-coated tablets are white to yellowish-white film-coated tablets, biconvex with no score-line.

[Nationally completed name] film-coated tablets are white to yellowish-white film-coated tablets, biconvex with score-line on one side.

NL/H/0328/001
Pack sizes: 20, 30, 50 or 100 film-coated tablets.

NL/H/0328/002
Pack sizes: 30, 50, 60 or 100 film-coated tablets.

Marketing Authorisation Holder and Manufacturer

Houder van de vergunning voor het in de handel brengen
Hexal AG
Industriestraße 25
D-83607 Holzkirchen
Duitsland

Fabrikant
Salutas Pharma GmbH
Otto-von-Guericke Allee 1
39179 Barleben
Duitsland

In het register ingeschreven onder:
RVG 27564 (25 mg)
RVG 27565 (50 mg)

This medicinal product is authorised in the Member States of the EEA under the following names:

Nederland: Azathioprine 25, 50 mg, filmomhulde tablet
Duitsland: Azathioprin - 1 A Pharma 25/50 mg Filmtabletten

Deze bijsluiter is voor het laatst goedgekeurd in juni 2021.

The following information is intended for healthcare professionals only:

Instructions for use and handling and disposal

There are no risks associated with handling tablets with intact coating. In that case no special safety precautions are necessary.

However, immunosuppressive agents should be handled in strict accordance with the instructions when nursing staff have halved the tablets (see sections 4.2 and 4.4 of the SmPC).

Surplus medical products as well as contaminated appliances should be temporarily stored in clearly labelled containers. Any unused product or waste material should be disposed of in accordance with local requirements.

Incompatibilities

Not applicable.

Administration

For oral use.
The tablet should be taken with at least a glass of liquid (200ml).

Shelf life

3 years

Special precautions for storage

This medicinal product does not require any special storage conditions.