

Package leaflet: Information for the patient

Imuran® 25 mg film-coated tablets

Imuran® 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, nurse 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, nurse or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

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

1. What Imuran Tablets are and what they are used for

Imuran Tablets 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.

Imuran Tablets 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).

Imuran Tablets 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.

Imuran Tablets 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 Imuran Tablets

Do not take Imuran Tablets:

- 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 Imuran Tablets).

Warnings and precautions

Talk to your doctor or pharmacist before taking Imuran Tablets

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

NUDT15-gene mutation

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

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

Your doctor will want to take **regular blood samples** while you are taking Imuran Tablets, to check for any changes (see section 3 "How to take Imuran Tablets"). The frequency of your blood tests will usually decrease the longer you continue to take Imuran Tablets. Your doctor may also perform genetic testing (i.e. looking at your TPMT and/or NUDT15 genes) before or during your treatment to determine if your response to this medication may be affected by your genetics. Your doctor may change your dose of Imuran after these tests.

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

- tumours, including skin cancer. Therefore, when taking Imuran Tablets, avoid excessive exposure to sunlight, wear protective clothing and use protective sunscreen with a high protection factor.
- lymphoproliferative disorders

- treatment with Imuran 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 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 Imuran Tablets, 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").

Pellagra

Talk to your doctor immediately if you experience diarrhoea, localized pigmented rash (dermatitis), decline in your memory, reasoning or other thinking skills (dementia) as these symptoms may suggest vitamin B3 deficiency (nicotinic acid deficiency/pellagra).

Other medicines and Imuran Tablets

Tell your doctor if you are taking, have recently taken or might take any other medicines. This is because Imuran Tablets can affect the way some medicines work. Also some other medicines can affect the way Imuran Tablets 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 Imuran Tablets. 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 Imuran Tablets.

Having vaccines while you are taking Imuran Tablets

If you are due to receive a vaccination (vaccine) speak to your doctor or nurse before you do so. If you take Imuran Tablets, 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 Imuran Tablets.

Imuran Tablets 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 have a baby, 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 Imuran Tablets. 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).

Breast-feeding

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

Fertility

The effects of Imuran Tablets on fertility are not known.

Driving and using machines

Imuran Tablets 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.

Imuran Tablets contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicinal product.

3. How to take Imuran 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 quantity of Imuran 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.

You can take Imuran 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 Imuran Tablets, this may be relieved by taking the tablets after food.

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

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

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 mg 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 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.

If you take more Imuran Tablets than you should

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

If you forget to take Imuran Tablets

Do not take a double dose to make up for a forgotten dose. 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 Imuran Tablets

Before you stop taking Imuran Tablets, consult with your doctor or pharmacist. Do not stop taking Imuran Tablets until your doctor tells you it is safe to do so.

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

4. Possible side effects

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

Stop taking Imuran Tablets 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 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 Imuran 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 up to 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 Imuran 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)
- 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 Imuran Tablets. Often hair does grow again, even if you carry on taking Imuran Tablets. 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)
- Pellagra (lack of vitamin B3 (niacin)) associated with pigmented rash; diarrhoea; or loss of memory.

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 HPRA Pharmacovigilance, Website: www.hpra.ie.

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

5. How to store Imuran Tablets

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

Do not store above 25 °C.

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

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.

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 Imuran Tablets contain

The active substance is azathioprine. Each Imuran 25 mg film-coated tablet contains 25 mg azathioprine. Each Imuran 50 mg film-coated tablet contains 50 mg azathioprine.

The other ingredients are:

Imuran 25 mg film-coated tablets contains the following excipients: lactose, maize starch, pregelatinised starch, stearic acid, magnesium stearate, hypromellose, macrogol, titanium dioxide (E171), iron oxide yellow (E172) and iron oxide red (E172).

Imuran 50 mg film-coated tablets contains the following excipients: lactose, maize starch, pregelatinised starch, magnesium stearate, stearic acid, hypromellose and macrogol 400.

What Imuran Tablets look like and contents of the pack

Imuran 25 mg film-coated tablets

Product imported from the the Netherlands:

Orange, circular tablets with 'L3C' on one side and plain on the other.

Product imported from Portugal

Orange, circular tablets with 'IM 2' on one side and plain on the other.

Imuran 50mg film-coated tablets

Product imported from the Romania:

Yellow, circular tablets with 'IM 5' scored on one side and plain on the other.

Product imported from Portugal and Romania

Yellow, circular tablets with 'GX CH1' scored on one side and plain on the other.

Imuran tablets are packaged in blister packs containing 50 or 100 film-coated tablets contained in an outer cardboard. Not all pack sizes may be marketed.

Manufacturer

Excella GmbH/Excella GmbH & Co. KG, Nürnberger Strasse 12, 90537 Feucht, Germany or Aspen Bad Oldesloe GmbH, Industriestrasse 32-36, 23843 Bad Oldesloe, Germany or GlaxoSmithKline Pharmaceuticals S.A., Ul. Grunwaldzka 189, 60-322 Poznan, Poland.

Product Procured from within the EU, repackaged and distributed by the Parallel

Product Authorisation Holder

PCO Manufacturing Ltd., Unit 10, Ashbourne Business Park, Rath, Ashbourne, Co. Meath, Ireland.

Product Authorisation Number

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Imuran 50 mg film-coated tablets PPA0465/077/002

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