

PACKAGE LEAFLET

Package leaflet: Information for the patient

Imuger 25 mg & 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 Imuger is and what it is used for
2. What you need to know before you take Imuger
3. How to take Imuger
4. Possible side effects
5. How to store Imuger
6. Contents of the pack and other information

1. What Imuger is and what it is used for

Imuger belongs to a group of medicines called immunosuppressants. Imuger helps to reduce or suppress your body's own immune system. It can be used together with other medicines such as corticosteroids to:

- help your body accept an organ transplant.

Imuger is also used to treat conditions where your immune system is reacting against your own body (autoimmune diseases) such as:

- rheumatoid arthritis (inflammation and pain in your joints)
- hepatitis (inflamed liver)
- inflammatory disease of the gut such as Crohn's disease or ulcerative colitis
- systemic lupus erythematosus (also known as 'lupus') 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)
- dermatomyositis (inflammation of your muscles and skin)
- polyarteritis nodosa (inflammation of your blood vessels)
- pemphigus vulgaris (severe blistering of the skin, mouth, nose, throat and genitals).

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

2. What you need to know before you take Imuger

Do not take Imuger 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)

Warnings and precautions

Talk to your doctor or pharmacist before taking Imuger if you:

- know you have a metabolic abnormality called Lesch-Nyhan syndrome. Imuger is not recommended if you have this condition.
- know you have a shortage of a liver enzyme called thiopurine methyltransferase (TPMT). TPMT breaks down Imuger and other medicines.
- have liver or kidney disease.
- have had hepatitis B (a liver disease caused by a virus).
- have an IUD fitted for contraception; as you will need an alternative form of contraception (see section 2 'Pregnancy and breastfeeding').
- have ever suffered from chickenpox or shingles.
- need to receive a vaccination.

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

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

Liver damage

Treatment with Imuger 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").

Chickenpox/Shingles infection

Infection with chickenpox or shingles can become severe in patients taking immunosuppressive medicine. Therefore you should avoid contact with anyone suffering from chickenpox or shingles.

Your doctor will monitor you closely throughout your treatment.

You will need to have your blood count checked at least once a week for the first two months of treatment and then monthly or at least 3 monthly.

Your doctor will monitor your blood count very closely if Imuger is given together with:

- allopurinol, oxipurinol or thiopurinol
- derivatives of aminosalicylic acid, such as mesalazine, olsalazine or sulfasalazine
- ACE inhibitors, co-trimoxazole,
- cimetidine
- indomethacin
- agents with cytotoxic/myelosuppressive properties (see section 'Other medicines and Imuger')

Your doctor will monitor you more regularly if you are elderly and on a high dose, or you have problems with your liver, kidney, immune system or spleen.

Withdrawal of Imuger will always be closely monitored by your doctor, as it is a gradual process to be performed.

Tell your doctor straight away if you suffer from mouth ulcers, fever, unusual bruising or bleeding of the skin, or suffer from more infections than usual. These effects may be due to blood changes (see section 4 ‘Possible side effects’).

Pellagra

Contact your doctor immediately if you have diarrhoea, localized pigmented rash (dermatitis), deterioration of your memory, reasoning and reasoning skills (dementia), as these symptoms may indicate a vitamin B3 deficiency (nicotinic acid deficiency/pellagra).

If the 50 mg tablets have to be halved, you must avoid contact between the skin and the broken portion of the tablet or the tablet dust (section 3 “How to take Imuger” and section 6 “Contents of the pack and other information”).

NUDT15-gene mutation

If you have an inherited mutation in the NUDT15-gene (a gene that is involved in the break-down of azathioprine in the body) you have a higher risk of infections and hair loss. Your doctor will monitor your blood count and may need to give you a lower dose.

Other medicines and Imuger

Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines, including medicines obtained without a prescription, or any of the following:

- other immunosuppressants e.g. ciclosporin, tacrolimus, methotrexate increase the risk of pronounced immunosuppression
- medicines to treat cancer may potentiate the myelotoxic effect
- penicillamine (for rheumatoid arthritis)
- allopurinol, oxipurinol or thiopurinol or other xanthine oxidase inhibitors e.g. febuxostat (mainly used to treat gout)
- anticoagulants to ‘thin’ the blood e.g. warfarin or acenocoumarol, its effect is inhibited by Imuger
- ACE inhibitors e.g. captopril (for blood pressure or heart failure, indometacin (an anti-inflammatory), cimetidine (for gut or stomach ulcers), co-trimoxazole (an antibiotic), ribavirin (to treat Hepatitis C) increase risk of myelosuppression
- infliximab (to treat Crohn’s disease)
- mesalazine, olsalazine or sulfasalazine (mainly used to treat ulcerative colitis); there is risk that Imuger may have an increased myelosuppressive effect
- the activity of Imuger can lead to an atypical and potentially harmful response to live vaccines.
- combination of Imuger and corticosteroids can diminish response of inactivated vaccines like hepatitis B vaccine.

Before a surgical procedure tell the anaesthesiologist that you are taking Imuger because muscle relaxants used during anaesthesia may interact with Imuger.

Pregnancy and breastfeeding

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Imuger **must not** be taken during pregnancy unless the benefits outweigh the risks.

Imuger may be prescribed during pregnancy only after the doctor has given careful consideration to the benefit versus risk ratio.

Both male and female patients should use effective contraception while using Imuger. This also applies to patients with impaired fertility due to chronic urine toxicity (uraemia), as fertility generally normalises following kidney transplantation. Reports indicate that certain contraceptives (intrauterine pessaries: coils, Copper T) may fail during treatment with Imuger. Please use other or additional contraceptive measures.

Your blood cell count should be checked regularly, as weakening of the immune system can occur in the newborn infants of mothers treated with Imuger during pregnancy.

Contact your doctor immediately if you experience severe itching without a rash during your pregnancy. You may also notice nausea and loss of appetite along with itching, indicating that you have a condition called pregnancy cholestasis (a disease of the liver during pregnancy).

Do not breastfeed during treatment with Imuger, as metabolic products produced in the body pass into the breast milk and can damage your child. If a decision is made to breastfeed, the breastfed infant should be closely monitored for signs of immunosuppression, blood or liver problems, severe pain in the abdomen or back (pancreatitis) or other symptoms of metabolic product exposure.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines

Imuger is not known to affect your ability to drive or use machines. If you are affected, do not carry out these tasks.

Imuger contains sodium

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

3. How to take Imuger

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

Your dose will be adjusted depending on your weight.

The recommended dose is:

Adults

To prevent organ rejection

The recommended starting dose is up to 5 mg/kg/day. Your doctor will then assess your response to Imuger and choose the best dose for you. The dose will usually be between 1 and 4 mg/kg/day.

Other conditions

The recommended starting dose is between 1 and 3 mg/kg/day. If you are being treated for hepatitis (an inflamed liver) the usual dose is between 1 and 1.5 mg/kg/day. Your doctor will adjust the dose until it is right for you. You will be given the lowest dose that is effective to treat your condition. If there is no improvement after three to four months, your doctor may stop giving you this medicine.

It may take several weeks or months for this medicine to take effect.

Elderly or patients 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 Imuger. Your doctor will monitor your blood and liver function tests carefully. Imuger should be given with special care to patients with severe liver problems (see section 2 'Do not take').

Use in children and adolescent under 18 years

Imuger is **not recommended** for the treatment of juvenile idiopathic arthritis, systemic lupus erythematosus, dermatomyositis and polyarteritis nodosa due to insufficient data.

As far as the other indications are concerned, the recommended dosages apply to children, adolescents and adults.

Children who are considered overweight may require a higher dose.

Taking Imuger

Swallow the tablets with a full glass of water (200 ml) and with meals (especially if you feel sick after taking your Imuger). Do not crush or chew the tablets.

You should take your medicine at least one hour before or two hours after having milk or dairy product. Do not break the tablets. If you do need to halve the 50 mg tablets, avoid skin contact with the broken half or any tablet dust.

If you take more Imuger than you should

Contact your doctor or nearest hospital emergency department **immediately**. Take the container and any remaining tablets with you. An overdose can cause a lack of white blood cells leading to frequent infections, fever, severe chills, sore throat or mouth ulcers. Other possible symptoms are tiredness, unusual bruising and bleeding of the skin, feeling and/or being sick and diarrhoea.

If you forget to take Imuger

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, do not double your next dose, carry on as usual and check with your doctor. If you miss more than one dose, check with your doctor.

If you stop taking Imuger

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

Withdrawal of Imuger, will always be closely monitored by your doctor as it is a gradual process to be performed (see section 2 'Warnings and precautions')

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 happens **stop taking Imuger and tell your doctor immediately or go to your nearest hospital emergency department:**

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

- Signs of a viral, fungal or bacterial infection. If you are taking Imuger after a kidney transplant, and with another immunosuppressant or corticosteroid, you may be more likely to catch infections.
- Reduction in white blood cells which may cause mouth ulcers, fever, chills, suffering more infections than usual. This is also more likely if your dose of Imuger is not reduced when taken with allopurinol, you have liver or kidney problems, or TPMT deficiency (see section 2 'Warnings and precautions').

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

- Reduction in blood platelets which increase the risk bleeding or bruising of the skin.

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

- Signs of a viral, fungal or bacterial infection are uncommon, if you have not had a kidney transplant, and are not taking another immunosuppressant or corticosteroid.
- Low red blood cell counts which can cause tiredness and pale skin
- Inflamed pancreas which causes severe pain in the abdomen and back
- Reduced flow of bile from the liver because of a blockage
- Abnormal liver function test

- Allergic reactions such as skin rash or red spots, feeling generally unwell, dizziness, feeling or being sick, diarrhoea, fever, chills, inflamed blood vessels, muscle or joint pain, kidney problems, raised liver enzymes in the blood, or a fall in blood pressure (hypotension) which may cause light-headedness or sweating. In severe cases this has resulted in death (very rare: may affect up to 1 in 10,000 people)
- Cholestasis of pregnancy, which may cause severe itching, especially of the hands and feet

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

- Various types of cancers including blood, lymph and skin cancers
- Severe reduction of all types of blood cells which can cause weakness, bruising or make infections more likely
- 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.

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

- Certain type of lymphoma (hepatosplenic T cell lymphoma). You may develop nose bleeds, fatigue, significant night sweats, weight loss and unexplained fever).
- Excessive breakdown of red blood cells causing tiredness and pale skin
- An inflamed bowel, abdominal pain, fever, discomfort, vomiting or diarrhoea. This is more likely to happen if you also take high doses of corticosteroids and following a transplant. Also, severe diarrhoea may happen, especially if you are being treated for inflammatory bowel disease.
- Memory loss, trouble thinking, difficulty with walking or loss of vision. This may be Progressive Multifocal Leukoencephalopathy (PML), a serious and life threatening brain condition.
- Severe blistering of the skin, mouth, throat, nose, genitals and conjunctivitis (red and swollen eyes).
- Inflammation of the lungs which can cause weakness, breathlessness, cough and fever.

Not known (frequency cannot be estimated from the 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).
- Sensitivity to light or sunlight.
- Pellagra (vitamin B3 [nicotinic acid] deficiency), associated with pigmented rash, diarrhoea, memory loss.

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

Other side effects include:

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

- Feeling or being sick

This is more likely at the start of treatment. Taking the tablets with food may help.

Rare (may affect up to 1 in 1000 people):

- Hair loss.

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 HPRC 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 Imuger

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 label/carton/blister after EXP.

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

Do not store above 25°C. Store in the original package.

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 Imuger tablets contain

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, croscarmellose sodium and sodium stearyl fumarate. The film-coating contains hypromellose and macrogol.

What Imuger tablets looks like and contents of the pack

The film-coated tablets are pale yellow and round. 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. The 50 mg tablets have a breakline and can be halved (see section 3 'How to take')

Imuger is available in blister packs of 20, 30, 50, 90 and 100 tablets or plastic containers of 20, 30, 50, 100, 500 and 1000 tablets. Not all pack sizes may be marketed.

Marketing Authorisation Holder

Viartis Limited, Damastown Industrial Park, Mulhuddart, Dublin 15, Dublin, Ireland

Manufacturers:

McDermott Laboratories Ltd. T/A Gerard Laboratories
35-36 Baldoyle Industrial Estate, Grange Road, Dublin 13, Ireland.

Delpharm Lille SAS

Parc d'Activites Roubaix-Est, 22 Rue de Toufflers, CS 50070, 59452 Lys-Lez-Lannoy, France.

Mylan Hungary Kft.

Mylan utca 1, Komárom 2900, Hungary.

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

Denmark:	Azatioprin Viartis 25 mg & 50 mg tablets
France:	Azathioprine Viartis 50 mg comprimé pellicule
Ireland:	Imuger 25 mg & 50 mg film-coated tablets
The Netherlands:	Azathioprine Viartis 25 mg & 50 mg

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