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

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 severe 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).

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)
- during a **pregnancy**, if the risks outweigh the benefits (see section 2 'Pregnancy and breast-feeding')
- while **breast-feeding** (see section 2 'Pregnancy and breast-feeding').
- have a severe infection
- have severe liver problems
- have a very weak immune system

- have an inflamed pancreas causing abdominal pain and sickness.

During treatment with Imuger live vaccines (particularly against tuberculosis, smallpox and yellow fever) may not be used.

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 an IUD fitted for contraception; as you will need an alternative form of contraception.
- have ever suffered from chickenpox or shingles.

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.

<u>Chickenpox/Shingles infection</u>
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’).

Male and Female patients of reproductive age must use contraception during Imuger therapy and for at least three months thereafter.

Imuger has been reported to interfere with the effectiveness of intrauterine contraceptive devices. Use alternative or additional contraceptive measures (see section 'Pregnancy and breast feeding').

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)
- furosemide ('water tablets') reduces metabolism of Imuger
- anticoagulants to 'thin' the blood e.g. warfarin or acenocoumarol, it's 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. (see section 2 'Do not take')
- 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 breast feeding
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.

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 of reproductive age should use contraception whilst taking Imuger and for at least 3 months after the end of treatment. 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.

Do not breast-feed during treatment with Imuger, as metabolic products produced in the body pass into the breast milk and can damage your child.

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.

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 not** be given 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.

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.
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):
- Inflamed pancreas which causes severe pain in the abdomen and back
- Liver problems causing dark urine, pale stools, yellowing of the skin or whites of the eyes. Imuger can cause a rare but severe form of liver disease, which can be fatal.
- Reduction in blood platelets which increase the risk bleeding or bruising of the skin.
- Vulva cancer (a type of cancer that affects the outer genital area in women).

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

Rare (may affect up to 1 in 1,000 people):
- Various types of cancers including blood, lymph and skin cancers
- 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
- Stomach or gut ulcers
- Bleeding from the gut, blood in the stools
- Severe reduction of all types of blood cells which can cause weakness, bruising or make infections more likely
- Inflammation of the lungs which can cause weakness, breathlessness, cough and fever.

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

Not known (frequency cannot be estimated from the available data):

- Kidney problems which may cause blood in the urine, a change in the amount of urine passed, and feeling drowsy or weak
- 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).

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:

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

- feeling or being sick
- loss of appetite.

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

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

- Pale skin, feeling weak or breathlessness.

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

- Diarrhoea
- Pale, greasy, offensive-smelling stools
- Hair loss.

Not known (frequency cannot be estimated from the available data):

- Stiff neck, sensitivity to bright light and headache.

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 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 25ºC. 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
McDermott Laboratories Ltd. T/A Gerard Laboratories
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This medicinal product is authorised in the Member States of the EEA under the following names:

Denmark:	Azatioprin Mylan 25 mg & 50 mg tablets
France:	Azathioprine Viatris 50 mg comprime pellicule sécable
Ireland:	Imuger 25 mg & 50 mg film-coated tablets
The Netherlands:	Azathioprine Mylan 25 mg & 50 mg

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