

Applicant: Pharmacare Ltd
Product name: IMURAN INJECTION
Dosage form and strength: Injection, 50 mg

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1.3.2 Patient Information Leaflet

SCHEDULING STATUS

S4

IMURAN INJECTION 50 mg

Azathioprine

Sugar free

Each vial contains 50 mg of azathioprine as the sodium salt.

The sodium ion content of the injection is approximately 4,5 mg (0,2 mEq)

Read all of this leaflet carefully before you are given IMURAN INJECTION

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor, pharmacist, nurse or other healthcare provider.
- IMURAN INJECTION has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

What is in this leaflet

1. What IMURAN INJECTION is and what it is used for
2. What you need to know before IMURAN INJECTION is given to you
3. How to use IMURAN INJECTION
4. Possible side effects

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5. How to store IMURAN INJECTION
6. Contents of the pack and other information

1. What IMURAN INJECTION is and what it is used for

IMURAN INJECTION contains the active substance azathioprine.

It belongs to a group of medicines called immunosuppressants. These medicines reduce the activity (strength) of your body's immune system. IMURAN INJECTION may be used on its own, but it is more often used in combination with other medicines.

IMURAN INJECTION is used to:

- stop your body rejecting an organ after an organ transplant,
- treat inflammatory bowel disease if the first line therapy has failed for you,
- treat diseases where your immune system reacts against your own body (called autoimmune diseases, such as rheumatoid arthritis).

2. What you need to know before IMURAN INJECTION is given to you

IMURAN INJECTION should not be administered to you:

- If you are hypersensitive (allergic) to azathioprine, 6-mercaptopurine or any of the other ingredients of IMURAN INJECTION (listed in section 6).
- If you are pregnant or planning to fall pregnant in the near future.
- If you are breastfeeding your baby.
- If you suffer from rheumatoid arthritis (a chronic progressive disease causing inflammation in the joints) and you have been treated with medicines referred to as alkylating medicines (e.g. cyclophosphamide, chlorambucil, melphalan or others).

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Warnings and precautions

Take special care with IMURAN INJECTION:

Tell your doctor or healthcare provider before being given the injection:

- if you have any kidney or liver 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 had hepatitis B (a liver disease caused by a virus),
- if you have an inherited mutation in the NUDT15-gene (a gene which is involved in the break-down of IMURAN INJECTION 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 have a genetic condition known as 'Lesch-Nyhan Syndrome'. This is a rare condition that runs in families caused by a lack of an enzyme called HPRT or 'hypoxanthine-guanine-phosphoribosyltransferase',
- when using IMURAN INJECTION, you are at a greater risk of developing other infections such as PML (Progressive Multifocal Leukoencephalopathy) which is an opportunistic infection. If you experience any signs of infection please contact your doctor,
- if you are receiving continuous IMURAN INJECTION together with corticosteroids you may have a persistent negative nitrogen balance. This means that the amount of nitrogen excreted from the body is greater than the amount of nitrogen ingested,
- if you are pregnant or are planning to have a baby, as IMURAN INJECTION can be unsafe and affect your baby,
- if you develop unexpected bruising or bleeding,

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- if you experience loss of appetite, nausea, vomiting or diarrhoea,
- when using IMURAN INJECTION, you are at a greater risk of developing tumours or other types of cancers such as lymphoproliferative disorder. With a treatment regime that contains more than one medicine that suppresses your immune system, this could lead to death,
- if you are taking a combination of multiple medicines that suppresses your immune system, it may increase your risk of developing disorders of the lymph system due to a viral infection (Epstein-Barr virus (EBV)-associated lymphoproliferative disorders),
- if you are exposed to sunlight and UV light. You should limit your time in the sun, wear protective clothing and use a sunscreen with a high protection factor as you are at a greater risk of developing skin cancer and skin sensitivity reactions while using IMURAN INJECTION,
- when using IMURAN INJECTION, you are at a 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,
- if you develop chickenpox or shingles. You should avoid contact with any person that has chickenpox or shingles.
- if you have recently received, or are due to receive a vaccination (vaccine). If IMURAN INJECTION is given to you, 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 given IMURAN.

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- 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. You should inform your anaesthesiologist of your treatment with IMURAN prior to surgery.

If you are receiving immunosuppressive therapy, IMURAN INJECTION could put you at greater risk of:

- Tumours, including skin cancer. Therefore, when taking Imuran injection, avoid excessive exposure to sunlight, wear protective clothing and use protective sunscreen with a high protection factor.
- Lymphoproliferative disorders
Treatment with IMURAN 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, avoid contact with people who have chickenpox or shingles.
- A previous hepatitis B infection becoming active again.

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- Other infections such as PML (Progressive Multifocal Leukoencephalopathy) which is an opportunistic infection. If you experience any signs of infection, please contact your doctor.

Tests you may have while using IMURAN INJECTION

Your doctor may ask you to have blood tests while you are using IMURAN INJECTION.

This is to check your blood cell count, liver and kidney function. Your doctor may change your dose of IMURAN INJECTION after the test or even stop IMURAN INJECTION.

Other medicines and IMURAN INJECTION

Always tell your healthcare provider if you have recently taken, are taking or might take any other medicine (this includes complementary or traditional medicines).

This is because IMURAN INJECTION can affect the way some medicines work.

Tell your doctor if you are taking or are planning to take any of the following:

- Vaccines. If you have recently received or are due to have a vaccination. If you take IMURAN INJECTION, 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 or pharmacist. This is because some vaccines may give you an infection if you receive them while you are taking IMURAN INJECTION.
- Ribavirin: medicine used to treat viral infections such as Respiratory syncytial virus (RSV) infection and hepatitis C.
- Xanthine oxidase inhibitors (e.g. allopurinol, oxipurinol, thiopurinol, febuxostat): medicine used to treat gout.

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- Neuromuscular blocking medicines (e.g. tubocurarine, curare, pancuronium, succinylcholine): medicines used during operations to relax muscles. You should inform your anaesthesiologist of your treatment with IMURAN INJECTION prior to surgery.
- Other medicines that suppresses the immune system (e.g. penicillamine): medicine used to treat rheumatoid arthritis.
- Trimethoprim/sulfamethoxazole (co-trimoxazole): medicine used to treat bacterial infections.
- ACE inhibitors (e.g. captopril): medicine used to treat high blood pressure or heart problems.
- Cimetidine: medicine used to treat stomach ulcers and indigestion.
- Indomethacin: medicine used to treat pain and inflammation.
- Furosemide: medicine used to treat high blood pressure or heart problems.
- Cytostatic medicines: medicines used to treat various types of cancer.
- Aminosalicylates (e.g. olsalazine, mesalazine or sulfasalazine): medicines mainly used in the treatment of ulcerative colitis and Crohn's disease.
- Methotrexate: medicine used to treat cancer and autoimmune diseases.
- Infliximab: medicine used to treat chronic inflammatory diseases (ulcerative colitis and Crohn's disease).
- Anticoagulants (e.g. warfarin, acenocoumarol): medicines used treat or prevent blood clots.

Pregnancy, breastfeeding and fertility

The safety of IMURAN INJECTION in pregnancy and lactation has not been established.



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If you are pregnant your doctor will carefully consider whether to give you IMURAN INJECTION.

If you are pregnant or breastfeeding, think you may be pregnant or are planning to have a baby, please consult your doctor, pharmacist or other healthcare provider for advice before being given IMURAN INJECTION.

Do not use IMURAN INJECTION if you are a man and trying to father a child. IMURAN INJECTION may affect the baby.

Small amounts of IMURAN INJECTION may pass into the breast milk. It is recommended that women receiving IMURAN INJECTION should avoid breastfeeding.

Reliable contraceptive precautions must be taken to avoid pregnancy whilst you or your partner is using IMURAN INJECTION.

The effects of IMURAN INJECTION on fertility are not known.

Driving and using machines

IMURAN INJECTION has a moderate influence on the ability to drive and use machines.

It is not always possible to predict to what extent IMURAN INJECTION may interfere with your daily activities. You should ensure that you do not engage in the above activities until you are aware of the measure to which IMURAN INJECTION affects you (see section 4).

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IMURAN INJECTION contains sodium

Each 50 mg vial of IMURAN INJECTION contains approximately 4,5 mg (0,2 mEq) sodium. This should be taken into consideration by patients on a sodium controlled diet.

3. How to use IMURAN INJECTION

IMURAN INJECTION is given as an intravenous injection (into a vein) or after dilution as an intravenous infusion (for a longer time). It will usually be given by your doctor or nurse. The amount of IMURAN INJECTION 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 are given IMURAN INJECTION, 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 INJECTION. High levels of uric acid may damage your kidneys.

Recommended dose of IMURAN INJECTION in 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 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:

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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.

Recommended dose of IMURAN INJECTION 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 to be overweight may require a higher dose.

You will not be expected to give yourself IMURAN INJECTION. It will be given to you by a person who is qualified to do so.

Your doctor will give you IMURAN INJECTION so it is unlikely that you will receive too much.

If you think you have been given too much or have missed a dose tell your doctor or nurse.

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

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If you use more IMURAN INJECTION than you should

Since a healthcare provider will administer IMURAN INJECTION, he/she will control the dosage. However, in the event of overdosage your doctor will manage the overdosage.

Overdosage with IMURAN INJECTION can cause infection, ulceration of the throat, bruising and bleeding.

If you forget to use IMURAN INJECTION

Since a healthcare provider will administer IMURAN INJECTION, it is unlikely that the dose will be missed.

4. Possible side effects

IMURAN INJECTION can have side effects.

Not all side effects reported for IMURAN INJECTION are included in this leaflet. Should your general health worsen or if you experience any untoward effects while taking IMURAN INJECTION, please consult your healthcare provider for advice.

If any of the following happens, stop using IMURAN INJECTION and tell your doctor immediately or go to the casualty department at your nearest hospital:

- swelling of the hands, feet, ankles, face, lips and mouth or throat, which may cause difficulty in swallowing or breathing,
- rash or itching,
- fainting,

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- blistering of the skin, mouth, eyes and genitals as these may be due to a serious allergic reaction known as Stevens-Johnson Syndrome (SJS) and detachment of the skin known as Toxic epidermal necrolysis (TEN).
- headache, nausea, vomiting, diarrhoea, tiredness, rash, fever, joint pain and liver inflammation.
- less common side effects include inflammation of the pancreas (pancreatitis), infections, lymphoma (cancer of the lymph nodes) and skin cancer.

These are all very serious side effects. If you have them, you may have had a serious reaction to IMURAN INJECTION. You may need urgent medical attention or hospitalisation.

Tell your doctor immediately or go to the casualty department at your nearest hospital if you notice any of the following:

- inflammation of the pancreas, which may cause you severe upper stomach pain, with nausea and vomiting,
- severe liver damage or failure which can be life threatening, which may cause pale stools, dark urine, itchiness and yellowing of your skin and eyes (jaundice),
- inflammation of your lungs causing breathlessness, cough and a fever,
- various types of tumours and cancers,
- problems with your blood and bone marrow which may cause weakness, tiredness, paleness, breathlessness, dizziness, bruising, bleeding or infections,
- blood in stools or vomiting blood due to perforation or bleeding of the bowel (this can be due to internal bleeding),
- changes in the way your heart beats, for example, if you notice it beating faster,

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- kidney failure with symptoms such as swelling of your ankles, painful urination, producing less urine than what is normal for you and blood in your urine.

These are all serious side effects. You may need urgent medical attention.

Tell your doctor if you notice any of the following:

Frequent side effects:

- infections caused by a virus, fungus or bacteria. Signs of infection such as a sore throat, fever or cough,
- nausea.

Less frequent side effects:

- abnormal blood tests showing how your liver and blood works,
- problems with your bowel leading to severe diarrhoea, stomach pain, constipation, nausea and vomiting,
- hair loss.

Side effects with an unknown frequency:

- abnormal levels of phosphate, nitrogen or uric acid in the blood, loss of appetite,
- headache, dizziness,
- damage to the retina of the eyes which may cause vision impairment,
- low blood pressure,
- discolouration of the fingers and/or toes after exposure to changes in temperature (hot/cold) (Raynaud's phenomenon),

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- vomiting, inflammation of the stomach or the tube running from the throat to the stomach (oesophagus), mouth sores, stomach pain,
- pigmentation of the skin and nails, sensitivity to light or sunlight (photosensitivity),
- muscle pains, joint pains,
- suppression of normal function of the ovaries and testicles causing the absence of periods and the inhibition of formation of sperm,
- abnormalities in chromosomes (e.g. Down syndrome),
- tiredness, fever, shivers, weakness.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

Reporting of side effects

If you get side effects, talk to your doctor, pharmacist or nurse. You can also report side effects to:

SAHPRA: <https://www.sahpra.org.za/health-products-vigilance/>

Aspen Pharmacare:

E-mail: Drugsafety@aspenpharma.com

Tel: 0800 118 088

By reporting side effects, you can help provide more information on the safety of IMURAN INJECTION.

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5. How to store IMURAN INJECTION

Store all medicines out of reach and sight of children.

Store at or below 25 °C.

Protect from light.

Keep in the original packaging until required for use.

Do not store in a bathroom.

Do not use after the expiry date stated on the label. The expiry date refers to the last day of that month.

Return all unused medicine to your pharmacist.

Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

6. Contents of the pack and other information

What IMURAN INJECTION contains

The active substance is 50 mg of azathioprine.

The other ingredients are sodium hydroxide and water for injection.

Before IMURAN INJECTION is injected it is diluted in sterile water.

What IMURAN INJECTION looks like and contents of the pack

Powder for solution for injection. IMURAN INJECTION is a yellow to amber freeze-dried powder, which when reconstituted is a clear, or slightly opalescent, yellow solution, essentially free from visible particles.

Glass vials containing the equivalent of 50 mg azathioprine as its sodium salt, freeze dried. The vials are fitted with a light grey bromobutyl rubber stopper and a



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polypropylene with aluminium flip-off seal. The sealed vial is packed into a preprinted carton together with a leaflet.

Holder of Certificate of Registration

PHARMACARE LIMITED

Healthcare Park

Woodlands Drive

Woodmead

2191

Hotline: 0800 118 088

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Registration number

H2746 (Act 101/1965)

Access to the corresponding Professional Information

SAHPRA Repository of Professional Information and Patient Information Leaflets:

<https://www.sahpra.org.za/pi-pil-repository/>

Aspen Pharmacare:

E-mail: Medinfo@aspenpharma.com

Tel: 0800 118 088



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Botswana:

IMURAN INJECTION 50 mg: B9317275 S2

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