

PATIENT INFORMATION LEAFLET

SCHEDULING STATUS

S4

ASOTRIM 50 mg TABLETS

Azathioprine

Read all of this leaflet carefully because it contains important information for you

ASOTRIM is available without a doctor's prescription. Nevertheless, you still need to use ASOTRIM carefully to get the best results from it.

- Keep this leaflet. You may need to read it again.
- Do not share ASOTRIM with any other person.
- Ask your health care provider or pharmacist if you need more information or advice.

What is in this leaflet

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

1. What ASOTRIM is and what it is used for

ASOTRIM 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. ASOTRIM may be used on its own, but it is more often used in combination with other medicines.

ASOTRIM 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 you take [PRODUCT NAME]

Do not take ASOTRIM:

- if you are hypersensitive (allergic) to azathioprine, 6-mercaptopurine or any of the other ingredients of ASOTRIM (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 have an infection.
- 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).

Warnings and precautions

Take special care with ASOTRIM if:

- 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 ASOTRIM 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 ASOTRIM, 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 taking continuous ASOTRIM 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 ASOTRIM can be unsafe and affect your baby.
- If you develop unexpected bruising or bleeding.
- If you experience loss of appetite, nausea, vomiting or diarrhoea.
- When using ASOTRIM, 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 ASOTRIM.

- When using ASOTRIM, 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 you take ASOTRIM, 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 ASOTRIM.
- 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 ASOTRIM. You should inform your anaesthesiologist of your treatment with ASOTRIM prior to surgery.
- If you are receiving immunosuppressive therapy, ASOTRIM could put you at greater risk of:
 - Tumours, including skin cancer. Therefore, when taking ASOTRIM, avoid excessive exposure to sunlight, wear protective clothing and use protective sunscreen with a high protection factor.
 - Lymphoproliferative disorders.

Treatment with ASOTRIM 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 ASOTRIM, 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.
- Your doctor may ask you to have blood tests while you are taking ASOTRIM. This is to check your blood cell count, liver and kidney function. Your doctor may change your dose of ASOTRIM after the test or even stop ASOTRIM.

Other medicines and ASOTRIM

Always tell your healthcare professional if you are taking any other medicine. (This includes all complementary or traditional medicines). ASOTRIM 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 ASOTRIM, 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 ASOTRIM.
- 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), medicines used to treat gout.
- 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 ASOTRIM 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.

ASOTRIM with food and/or drink

ASOTRIM should be taken at least one hour before or three hours after food or milk.

Pregnancy and breastfeeding

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 health care provider for advice before taking ASOTRIM.

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

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

Small amounts of ASOTRIM may pass into the breast milk. It is recommended that women taking ASOTRIM should avoid breastfeeding.

Reliable contraceptive precautions must be taken to avoid pregnancy whilst you or your partner is taking ASOTRIM. The effects of ASOTRIM on fertility are not known.

Driving and using machines

It is not always possible to predict to what extent ASOTRIM may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which ASOTRIM affects them.

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

3. How to take ASOTRIM

Do not share medicines prescribed for you with any other person.

Take ASOTRIM exactly as described in this leaflet or as your doctor, pharmacist or nurse has told you. Check with your doctor or pharmacist if you are not sure.

ASOTRIM should be taken at least one hour before or three hours after food or milk.

Recommended dose of ASOTRIM 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:

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 ASOTRIM 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.

Your doctor will tell you how long your treatment with ASOTRIM will last. Do not stop treatment early because ASOTRIM may take a long time before improvement is noticed. If you have the impression that the effect of ASOTRIM is too strong or too weak, tell your doctor or pharmacist.

If you take more ASOTRIM than you should

In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison centre.

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

If you forget to take ASOTRIM

Do not take a double dose to make up for forgotten individual doses.

4. Possible side effects

ASOTRIM can have side effects.

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

If any of the following happens, stop taking ASOTRIM 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.
- Fatigue (feeling tired).
- 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 ASOTRIM. 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.
- 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 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).
- 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 or pharmacist. You can also report side effects to SAHPRA via the “6.04 Adverse Drug Reaction Reporting Form”, found online under SAHPRA’s publications: <https://www.sahpra.org.za/Publications/Index/8>.

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

5. How to store ASOTRIM

STORE ALL MEDICINES OUT OF REACH OF CHILDREN.

Store well-closed below 25 °C and protect from light and moisture.

Store blister packed tablets in the original container below 25 °C and protect from light and moisture.

Do not use after the expiry date printed on the carton and blister.

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 ASOTRIM contains

- The active ingredient is azathioprine.
- The other ingredients are:

Tablet core

- Microcrystalline cellulose (PH 101)
- Mannitol
- Maize starch
- Povidone K25
- Croscarmellose sodium
- Sodium stearyl fumarate

Coating

- Methylhydroxy propyl cellulose E15

- Propylene glycol

What ASOTRIM looks like

ASOTRIM is pale yellow, round, biconvex tablet marked AE50 on one side and G on the reverse.

ASOTRIM is packed in white HDPP containers containing 100 tablets.

It is also packed in PVC/Aluminium blisters of 10 tablets per blister in unit cartons of 100 tablets.

Holder of Certificate of Registration

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