



PATIENT INFORMATION ON AZATHIOPRINE

(Brand names: Azamun, Azapin, Imuran, Thioprine)

This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- **how you should take your medicine**
- **the possible side effects**
- **what tests you must have to monitor your condition and to detect unwanted effects**
- **other precautions you should take while taking azathioprine.**

Please read it carefully and discuss it with your doctor.

Important things to remember

- While taking azathioprine you should see your rheumatologist regularly to make sure the treatment is working and to minimise any possible side effects.
- You should have regular blood tests as directed by your rheumatologist.
- If you are concerned about any side effects, you should contact your rheumatologist as soon as possible.

For more information about **RHEUMATOID ARTHRITIS** and other inflammatory conditions see Arthritis Australia's website: www.arthritisaustralia.com.au

What is azathioprine?

Azathioprine (brand names: Azamun[®], Azapin[®], Imuran[®], Thioprine[®]) is a medicine used to treat immune and inflammatory diseases such as vasculitis, systemic lupus erythematosus (SLE/lupus), polymyositis (muscle inflammation), rheumatoid arthritis and other rheumatic and autoimmune conditions.

Azathioprine is also used to prevent the rejection of transplanted organs and to treat inflammatory bowel disease such as Crohn's Disease or Ulcerative Colitis

Azathioprine is an immunosuppressive medicine, which means that it works by reducing the activity of the immune system. In rheumatoid arthritis this action helps to reduce inflammation and thus reduce pain and swelling. It also limits damage to the joints and helps to prevent disability in the long term.

Because azathioprine acts to reduce the damage to the joints, rather than just relieve the pain, it belongs to the group of medicines called **disease modifying antirheumatic drugs (DMARDs)**.

What benefit can you expect from your treatment?

Azathioprine does not work straight away. It usually takes 6 to 8 weeks for symptoms such as swelling and stiffness to start to improve. The effects to delay or prevent joint damage will take several months to be noticed. Other medicines may be given to improve your symptoms while waiting for azathioprine to work.

If you stop your azathioprine treatment for more than a few weeks there is a risk that your condition may worsen.

Treatment with azathioprine may be continued indefinitely as long as it is effective and no serious side effects occur.

How is azathioprine taken?

Azathioprine is taken by mouth in 25mg or 50mg tablets which should be swallowed whole. Breaking or crushing of tablets should be avoided.

What is the dosage?

The dose will depend on your particular immune or inflammatory condition, and is adjusted depending on your body weight. It is usually started at 50mg to 100mg per day. The dose can be increased every 1 to 2 months. The maximum dose can be up to 250mg per day.

Azathioprine can be taken as a once or twice a day.

Can other medicines be taken with azathioprine?

Azathioprine may be used with most other arthritis medicines including:

- other DMARDs
- steroid medicines such as prednisolone or cortisone injections into the joint
- anti-inflammatory medicines (NSAIDs) such as naproxen (Naprosyn) or ibuprofen (Brufen, Nurofen)
- simple pain medicines such as paracetamol.

There are separate information sheets for the medicines mentioned above.

Are there any side effects?

You might experience with your treatment. Tell your doctor if you are concerned about possible side effects.

A reduction in dose may minimise the side effects so that you can continue to take this treatment. Your doctor will advise on any dose changes that are necessary.

Most common possible side effects

- 10-15% of people taking azathioprine experience stomach or bowel side effects, which might include *nausea (feeling sick), vomiting, abdominal pain or diarrhoea*. Taking azathioprine twice a day instead of all at once, or taking it after eating, may help avoid these problems. Antinausea tablets can be used if needed.
- About 5% of people have side effects such as *skin rashes and increased sensitivity to the sun*. It is a good idea to use sunscreen and to wear a hat when out in the sun.

Less common or rare possible side effects

- *Effects on the liver and pancreas:* azathioprine can cause liver test abnormalities or hepatitis (inflammation of the liver). This occurs in less than 1% of

people taking the medicine. This does not cause symptoms unless severe so regular blood tests are important.

If you develop symptoms such as yellow discolouration of the whites of your eyes or yellow skin tell your doctor straight away. Azathioprine can also cause pancreatitis (inflammation of the pancreas), which can result in abdominal pain.

- *Blood counts:* azathioprine can cause a drop in the number of white blood cells, which are needed to fight infection. It can also cause a drop in the number of platelets, which help to stop bleeding.

Regular blood tests aim to pick these problems up early when they occur. However, if you develop a sore mouth, mouth ulcers, easy bruising, nosebleeds, bleeding gums, breathlessness, infection or fever tell your doctor straight away.

- *Hypersensitivity:* A small number of people have a hypersensitivity reaction one to two weeks after starting azathioprine. This causes sudden onset muscle aches and pains and fever. If you develop any of these symptoms tell your doctor straight away.
- *Infections:* There is an increased risk of developing some infections, especially herpes zoster (chicken pox and shingles). You should try to avoid contact with people who have these infections. If you have an infection or persistent fever, tell your doctor straight away.
- *Cancer:* Studies of transplant patients taking azathioprine have found it may increase risk of skin cancers. There may be a similar risk in people with rheumatic conditions who take azathioprine for long periods of time. You should discuss this issue with your rheumatologist before starting the medicine (see *Precautions* on page 4).
- There are also increased risks of other solid organ cancer or lymphoproliferative disorders depending upon the degree and duration of immune suppression

What precautions are necessary?

Blood tests

- Before starting azathioprine you may be asked to have a blood test to look at an enzyme (TPMT). This will check whether your bone marrow cells are more sensitive to the medicine. The result will decide whether this treatment is suitable for you and whether you should use a lower dose.

- Since the liver and blood cells may be affected by azathioprine, you **must** have regular blood tests during your treatment. This is very important as you may not get symptoms of these problems.
- Blood tests are particularly important during the first few months of treatment.
- As well as monitoring for side effects, blood tests help to monitor your condition to determine if the treatment is effective.
- You will need to have full blood counts and liver function tests every 2 to 4 weeks for the first few months of treatment and then every 1 to 3 months after that.
- If there are no abnormalities seen after 3 months of treatment at a specific dose of azathioprine, the blood tests may be done less frequently.
- Your general practitioner will be informed about the monitoring schedule. It is important to see your general practitioner if you have been asked to do so as they have an important role to play in monitoring your condition.

Use with other medicines

- Azathioprine can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all medicines you are taking or plan to take. This includes over the counter or herbal/naturopathic medicines.
- Allopurinol (Allohexal, Allosig, Pro gout, Zyloprim), used in the treatment of gout, will increase the level of azathioprine in the blood. Taking allopurinol with azathioprine can therefore be very dangerous. You must tell your doctor if you are taking or are advised to take allopurinol. If azathioprine is taken with allopurinol its dose needs to be very carefully reviewed.
- Febuxostat (Adenuris) is also used to treat gout and will increase the level of azathioprine in the blood. You must tell your doctor if you are taking or are advised to take febuxostat. If azathioprine is taken with febuxostat its dose needs to be very carefully reviewed.
- Anticoagulants (blood thinners) Eg Warfarin (brand names Coumadin, Marevan), inhibition of blood thinning effect of Warfarin has been reported. Coagulation should be closely monitored. You must tell your doctor if you are taking blood thinning tablets

- Combined pain medicines such as Panadeine and Panadeine Forte can be used safely with azathioprine provided you take them as directed.

Azathioprine can also be used safely with anti-inflammatory drugs (NSAIDs) as long as your kidney function is normal.

- If you are on azathioprine it is recommended you should not be immunised with 'live' vaccines such as MMR (measles, mumps and rubella), OPV (oral polio vaccine), BCG (Bacillus Calmette Guerin) or yellow fever. Talk to your doctor before receiving any vaccines.

Use with alcohol

- Because azathioprine can affect your liver, you should avoid heavy alcohol use while taking it.
- It is not known precisely what level of drinking is safe when on azathioprine. However, there is general agreement that 1 to 2 standard drinks taken once or twice a week is unlikely to cause a problem.
- Drinking more than 4 standard drinks on one occasion, even if infrequently, is strongly discouraged.

Use in pregnancy and breastfeeding

- Azathioprine has been used safely in pregnancy and breastfeeding.
- Should you wish to become pregnant or you intend to breastfeed, you should discuss this with your doctor.
- More detailed information is available at <https://rheumatology.org.au/gps/documents/ARAPregnancyPrescribingGuidanceupdateApr19.pdf>

Skin cancer prevention

- When taking azathioprine, it is important to use sunscreen and avoid prolonged sun exposure. A yearly skin check is recommended.

How to store azathioprine

- Store azathioprine in a cool, dry place, away from direct heat and light (e.g. not in the bathroom).
- Keep all medicines out of reach of children.

Questions?

If you have any questions or concerns write them down and discuss them with your doctor.

Your doctor's contact details

If you are taking azathioprine you should see your rheumatologist regularly to make sure the treatment is working and to minimize any possible side effects.

The information in this sheet has been obtained from various sources and has been reviewed by the Australian Rheumatology Association. It is intended as an educational aid and does not cover all possible uses, actions, precautions, side effects, or interactions of the medicines mentioned. This information is not intended as medical advice for individual problems nor for making an individual assessment of the risks and benefits of taking a particular medicine. It can be reproduced in its entirety but cannot be altered without permission from the ARA. The NHMRC publication: *How to present the evidence for consumers: preparation of consumer publications* (2000) was used as a guide in developing this publication.