

## Azathioprine factsheet

Azathioprine is a drug that was originally developed to prevent graft rejection in transplant patients. It has been available since the 1960s and has been used for many years to treat severe eczema. Clinical trials in the 1990s provided good evidence that azathioprine is effective for resistant moderate-to-severe disease. It has also frequently been used in other skin diseases as a means of reducing oral steroid use. However, azathioprine is not licensed for use in atopic eczema and is prescribed 'off-license' by dermatologists.

### How does azathioprine work?

Azathioprine is an immunosuppressant drug that is also known as an antimetabolite. It interferes with the growth of certain types of white blood cells (lymphocytes) that are involved in creating the inflammation associated with eczema. It takes a little longer to work than ciclosporin – it can take 2 to 3 months for an improvement to be seen – so it is less suitable for acute flares. Further improvements then occur over the next few months.

### When is azathioprine used?

Azathioprine is mainly used in the UK to treat people with severe atopic eczema that is unresponsive to conventional topical treatments. The reasons for prescribing azathioprine are similar to those for ciclosporin, although it is less suitable for acute flares because it takes longer to take effect. Azathioprine is available as 25 mg and 50 mg tablets. The dose is calculated based on the patient's weight. For patients with normal thiopurine methyltransferase, azathioprine can be taken as a single dose. But if side effects such as sickness occur, dividing the dose and taking it twice a day may help. A starting dose of 2 mg/kg is often used initially, and then the dose is gradually increased according to the response. The usual maintenance dose is between 100 mg and 250 mg per day (2.5 mg/kg per day).

### What are the side effects?

It is important to remember that most patients do not experience significant side effects. Blood tests will be taken before treatment to assess the individual risk for developing side effects. The main side effect concern with azathioprine is bone marrow suppression. This can result in severe anaemia and risk of infection. A blood test is now available to determine which patients are most at risk of developing this side effect with azathioprine. About 1 in 200 people have very low levels of an enzyme called thiopurine methyltransferase (TPMT). They are unable to break down azathioprine in the normal way and are at high risk of dangerous bone marrow suppression. **These patients should not receive azathioprine.** A further group of patients who have intermediate activity of TPMT may be given azathioprine, but it is recommended that a reduced dose be given, starting at 0.5 mg/kg and increasing to 1.0 mg/kg. If the level of TPMT is normal, risk of developing side effects is low. All patients taking azathioprine require regular blood tests before and during treatment to check for any signs of bone marrow suppression even if their TPMT level is normal. You should seek medical advice if you become unwell or develop signs of infection. It is important to report any unusual bruising or bleeding, which may be a sign that the bone marrow is being affected.

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Azathioprine can sometimes cause problems with the liver. Liver function tests are therefore performed at the start of treatment, with weekly monitoring to begin with. Once the patient is stable on a fixed dose of azathioprine, they will require blood tests every 3 months.

Nausea, diarrhoea and loss of appetite may be a problem for some patients, but this usually responds to a reduction in dose.

Hair loss can occur, but this is usually mild and reversible on stopping the drug.

Occasionally, a drug hypersensitivity syndrome may develop – this feels like ‘flu’ with aches, joint pains and fever. If this occurs, the drug should be stopped immediately and the prescribing doctor informed. Take a Covid-19 test, as some of the symptoms are similar.

Taking azathioprine for a number of years may increase your risk of developing skin cancer and a type of blood cancer called lymphoma. Protect yourself from sunlight by wearing sun protective clothing (such as long sleeves and a sunhat) and using sunscreen with a sun protection factor (SPF) of at least 30 and a star rating of at least 4. Avoid sunbathing.

### Can azathioprine be used in combination with other drugs?

Certain tablets increase the risk of side effects with azathioprine and should therefore be avoided. If any new tablets are considered, it is important to let the doctor know you are taking azathioprine. Allopurinol and Febuxostat, medications to treat gout, should not be taken with azathioprine. Warfarin (used to thin the blood) and some antibiotics (such as Septrin and Trimethoprim) should be avoided too. Some blood pressure tablets (those that are angiotensin-converting enzyme (ACE) inhibitors) should also be avoided.

### What blood tests are needed?

All patients taking azathioprine require blood tests before and during treatment to check for any signs of bone marrow suppression, even if their TPMT level is normal.

As azathioprine can sometimes cause problems with the liver, blood count and liver function tests will be carried out.

Patients will require blood tests once a week for the first month of treatment and then blood tests once a month. Once the patient is stable on a fixed dose of azathioprine, they will require blood tests every 3 months.

You should seek medical help if you develop a high fever or experience unexplained bruising or yellowing of the skin.

### Who is prescribed azathioprine?

Azathioprine can be prescribed for adults and older children with severe eczema, but only under consultant dermatologist supervision.

### Pregnancy and breastfeeding

If you are pregnant, planning to become pregnant or breastfeeding, this should be discussed with your doctor before taking azathioprine.

Azathioprine should not be used in pregnancy without careful assessment of the risks and benefits. There is no definitive evidence that azathioprine is harmful in pregnancy. However, some studies have shown an association with premature birth and small-for-date babies.

Azathioprine does not affect sperm quality or male fertility.

### Can I drink alcohol while taking azathioprine?

Alcohol can be consumed but it is advisable to keep consumption to a minimum, as both alcohol and azathioprine can affect the liver. The national guidelines for safe consumption recommend that men and women drink no more than 14 units a week.

### Immunisations and azathioprine

- *Covid-19 vaccines* available at the time of writing (2021) are safe for people on azathioprine.
- The 'live' vaccines such as MMR (measles, mumps, rubella), polio, chickenpox/shingles and yellow fever are no longer considered inappropriate for people taking azathioprine. However, the guidelines advise that your suitability for these vaccines should be decided by your doctor on an individual basis.
- *Chickenpox (Varicella zoster)*. If you have never had chickenpox, your doctor may recommend vaccination against it before starting azathioprine. If this was not possible and you come into contact with a person with chickenpox or shingles while you are taking azathioprine, you should go to your doctor straight away as you may need special preventative treatment.
- *Yearly influenza and 5-yearly pneumococcal injections* are safe and should ideally be given to everybody on azathioprine.

**If you have any questions or concerns, please do not hesitate to speak to the doctor, pharmacist or nurse caring for you.**

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