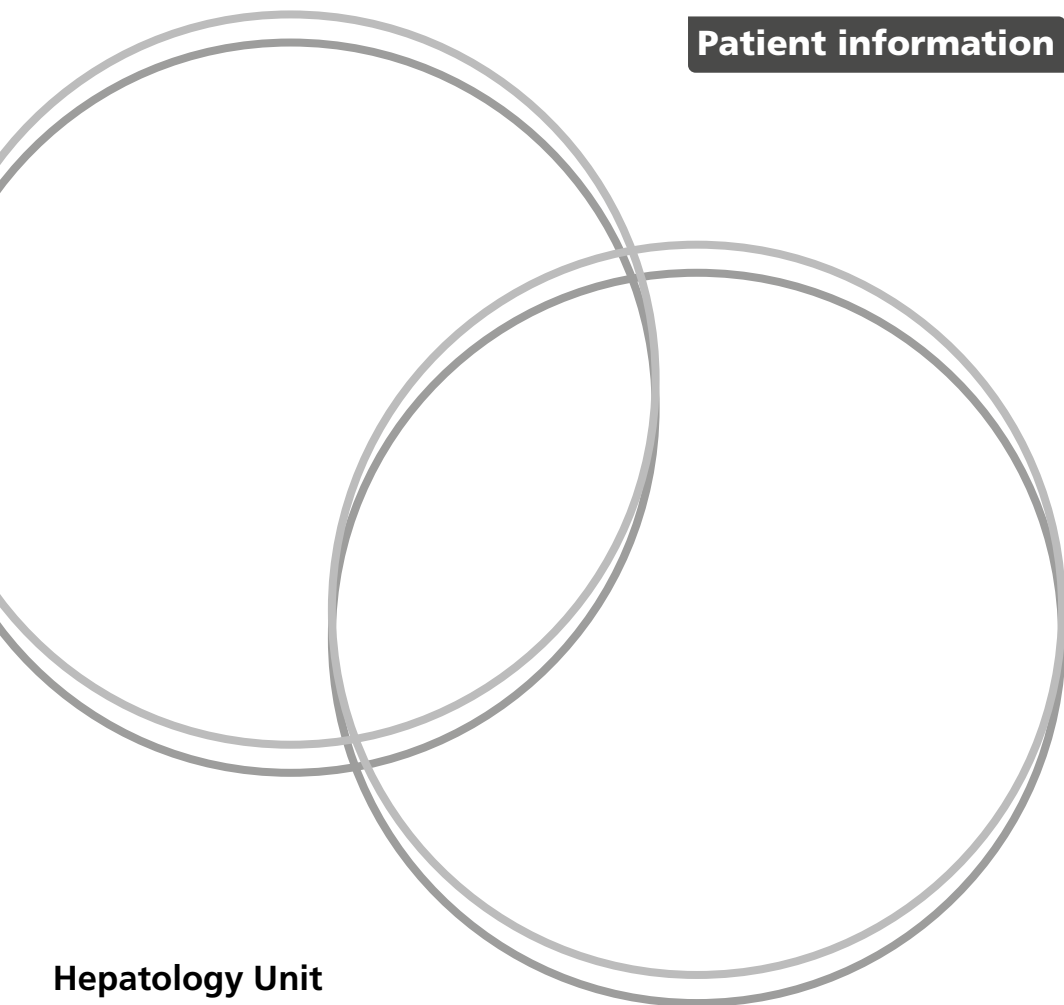




Oxford University Hospitals
NHS Foundation Trust

Azathioprine in autoimmune liver disorders

Patient information



Hepatology Unit

Azathioprine in autoimmune liver disorders

This leaflet answers some common questions patients ask about azathioprine.

Further information can be found in the information leaflet supplied by the manufacturer or from your pharmacist, liver nurse specialist or doctor.

Why have I been started on this medicine?

Azathioprine (also known as Imuran®, Azapress®) is prescribed for patients diagnosed with AIH (autoimmune hepatitis) and IgG4-related disease affecting liver/bile ducts and pancreas. These conditions are examples of an immune mediated (autoimmune) liver disorders.

Autoimmune liver disorders can develop when your body's own immune system mistakenly attacks the cells in your liver causes damage. No one knows why this happens. If left untreated it can lead to cirrhosis (scarring of the liver), which has a higher risk of liver cancer.

AIH may have an inherited predisposition to the disease, which is finally triggered by something in the environment. We do not, however, know what the environmental trigger is (or triggers may be). 30-50% of people diagnosed with AIH have another autoimmune condition, such as thyroid disease, rheumatoid arthritis, ulcerative colitis or Type 1 diabetes. It is estimated that 15 to 25 per 100,000 people in Europe have AIH.

IgG4 related disease is a chronic-fibroinflammatory disorder affecting a wide range of organs. Although these are commonly the salivary glands, pancreas, and bile duct and liver, aorta and retroperitoneum. It is a rare disease affecting an estimated 10 per 100,000 people.

Common symptoms associated with autoimmune liver disorders include fatigue, weight loss, nausea, abdominal pain, jaundice, dark urine. Because of related conditions, some people may have joint pains, diarrhoea and feel generally unwell. Most patients with well-controlled disease have no symptoms at all.

There is no cure for autoimmune liver disorders but there are effective treatments to control the disease and reduce the risk of progression including steroids, azathioprine and mercaptopurine. The main goal of treatment is to stop the liver inflammation by getting your immune system back under control. We can assess this with blood tests and imaging of the liver. Around 70% of patients will relapse within 12 months if treatment is withdrawn.

How does it work?

Azathioprine suppresses inflammation in the liver and 'turns off' the activity of the immune system (hence known as an 'immunomodulator'). Azathioprine is usually used in combination with a steroid e.g., prednisolone.

Reducing inflammation in the liver will improve your symptoms, improve your liver blood tests, reduce the degree of scarring and help prevent long-term liver damage and liver failure.

How long does it take to work?

Azathioprine can take several weeks to work unlike a steroid.

What dose do I take?

AIH and IgG4-RD: The recommended dose of azathioprine is initially 50mg/day which is usually started after you have started steroid treatment and continued with the steroid. The dose will be increased depending on response and side effects up until a maintenance dose of 1-2mg/kg (typically 50-150mg/day).

How do I take it?

Azathioprine comes in tablet form and is available in two different strengths (25mg and 50mg). It is important that you take the correct combination if more than one strength of tablet is supplied to make up a dose. The dose should be taken once a day and with, or soon after food as it can cause stomach irritation if taken on an empty stomach.

How long will I be taking it?

If tolerated, you will remain on azathioprine for at least 2 years and for at least 12 months after normalization of blood tests (liver transaminases and IgG).

Steroid-free monotherapy with azathioprine (or alternatively mercaptopurine or mycophenolate if not tolerated) is the goal of maintenance therapy. Patients can remain on azathioprine for many years (>5 years), and the risks and benefits of continuing the medication is constantly assessed.

What happens if I forget to take a dose?

If you remember within 12 hours, take your dose as normal. If more than 12 hours has elapsed, then forget that day's dose and take your next dose at the normal time. Do not double the dose. If you take too much azathioprine, tell your GP or contact the hepatology team as soon as possible.

What are the common side effects?

During early weeks of treatment, azathioprine may cause nausea and loss of appetite, rash, flu-like illness with fever and generalized aches and pains. You may notice some hair loss while taking azathioprine. However, hair often does grow again, even if you carry on taking it. Sometimes azathioprine may inflame the liver further or result in acute abdominal pain due to inflammation of the pancreas (a digestive gland in the abdomen). Most patients (75%) however, can take azathioprine without any of these side effects.

Azathioprine has been reported to cause blood disorders leading to weakness or breathlessness, a susceptibility to infections, and a tendency to bruise easily.

Azathioprine can increase the risk of skin cancer. You should avoid excessive exposure to sunlight and UV light, apply high factor sunscreen and wear protective clothing when outside. The use of sunbeds should be avoided.

What do I do if I experience side effects?

If you experience any signs of illness or side effects such as unexplained bruising, bleeding, or signs of infection such as sore throat, fever, cough, shortness of breath, malaise, development/ worsening yellowness of the skin or whites of the eyes, or severe itching contact your GP or liver specialist team as soon as possible.

Do I need any special checks while on azathioprine?

You will be under the specialist care of a hepatology consultant. When you are first diagnosed, you may require frequent outpatient appointments (every 2 weeks) so that we can adjust your medication and monitor your disease closely. Once your disease is well-controlled, your outpatient appointments and blood tests will become less frequent (every 3-6 months). It is important that you attend your appointments and have any tests that are recommended because they are vital to your care.

If you develop scarring of the liver (cirrhosis), you will have an ultrasound scan of the liver every six months. These ultrasound scans are important because people with cirrhosis have increased risk of liver cancer, and regular scans can help to detect liver cancer at an early and treatable stage.

Before you start azathioprine, we will take a blood test called TPMT. This measures the enzyme in your body responsible for breaking down azathioprine. It is known that some people have lower levels of TPMT than others, while some people have none. If you have a low level, you will need a lower dose of azathioprine to reduce the risk of side effects. If you have no TPMT you should not take azathioprine.

It is important that you have regular blood tests to check for early signs of changes in the blood. It is recommended that this is done every 2 weeks for the first month then at 1 monthly intervals for 3-months and then at 3-monthly intervals.

You should be offered hepatitis A and B vaccination if not protected and at risk.

If you have not had chicken pox before and come into personal contact with someone who has chickenpox or shingles, you must see a doctor as soon as possible.

We will do our best to keep the monitoring of your condition up to date. We strongly encourage you to become familiar with the tests you need, however, to ensure these tests happen when they should.

Does azathioprine interfere with my other medicines?

Azathioprine can interact with other medicines, for example allopurinol, trimethoprim and co-trimoxazole. Always check with your doctor or pharmacist first.

It is safe to drink alcohol in moderation whilst on azathioprine, but it may aggravate the nausea. You will be advised not to drink alcohol if you have advanced fibrosis or liver cirrhosis.

You should avoid having 'live' vaccines whilst taking azathioprine e.g, Mumps, measles and rubella (MMR), yellow fever, BCG, some Typhoid vaccines, Varicella vaccines. If you require travel vaccines or your doctor, nurse or pharmacist advise that you need a vaccine always tell the healthcare professional that you are taking azathioprine. Seasonal vaccination against influenza, Pneumococcal and COVID vaccines are also recommended for adults taking azathioprine.

Is azathioprine OK in pregnancy and breastfeeding?

There is no evidence that azathioprine increases the risk of miscarriage, still birth or congenital abnormality. It is generally advised that azathioprine is continued to minimise the risk of relapse in the mother. Evidence has shown that the benefits of breastfeeding outweigh any theoretical risks of taking azathioprine. The daily dose should be taken after a feed.

If you are planning to become pregnant or unexpectedly fall pregnant whilst taking azathioprine, please discuss with the hepatology team. Do not abruptly stop taking the azathioprine as this can lead to a flare.

Where can I receive more information and support?

Hepatology pharmacist:

Tel: **01865 22 1523**

Hepatology Nurse advice line:

Tel: **01865 22 2057**

AIH Support

Help for those affected by Autoimmune Hepatitis: AIH Support

British Liver Trust:

British Liver Trust Helpline:

Tel: **0800 652 7330**

(10:00 to 15:00 Monday to Friday)

UK-AIH:

UK-AIH

Keep all medicines out of the reach of children.

Never give any medication prescribed for you to anyone else.

It may harm them even if their symptoms are the same as yours.

Further information

If you would like an interpreter, please speak to the department where you are being seen.

Please also tell them if you would like this information in another format, such as:

- Easy Read
- large print
- braille
- audio
- electronic
- another language.

We have tried to make the information in this leaflet meet your needs. If it does not meet your individual needs or situation, please speak to your healthcare team. They are happy to help.

Authors: Version 1 Sarah Cripps, Consultant Pharmacist, June 2022
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