INFORMATION SHEET AZATHIOPRINE / 6-MERCAPTOPURINE TREATMENT FOR GASTROENTEROLOGY PATIENTS

What are they? Azathioprine and 6-Mercaptopurine (6-MP) are immunosuppressant drugs used in the treatment of inflammatory bowel disease and autoimmune liver diseases. They are often prescribed when steroids have proved insufficient in bringing (or maintaining) the condition under control. They allow a reduction in the dose of steroids, but may take at least 12 weeks or more to become effective.

How is it taken? In tablet form, daily. The usual dose is 2 - 2.5 mg per kg bodyweight. The exact dosage will be advised by your Gastroenterology specialist.

Are there any side effects? These drugs are an important part of the treatment of patients with inflammatory bowel or autoimmune liver disease, but a small number of patients may experience side effects that could prevent them from continuing with treatment. Should you develop symptoms that might be related to your treatment you should discuss them with your GP / Gastroenterologist.

Possible side effects include:

- Nausea / vomiting and loss of appetite
- Abdominal pain: Severe abdominal pain due to an inflamed pancreas (pancreatitis) can occur with Azathioprine. If this happens the drug should be stopped immediately, but your doctor will advise you on what to do.
- Hair loss
- Adverse effects on the blood: Azathioprine can suppress your bone marrow, which is responsible for producing your red and white blood cells. This means that you could become anaemic or you may become less able to fight **infections** (!). You can help to detect if this has happened by letting your GP know if you develop a sore throat, fever, chills or flu like symptoms as well as unusual bruising or bleeding. Also tell your doctor if you develop cold sores or shingles, or come into contact with someone suffering from chicken pox or shingles. Your GP can check your blood and treat you if necessary.
- Fever, weakness and fatigue, muscle and joint pain (rare)
- Rarely, patients may be allergic to azathioprine. This causes severe 'flu'-like symptoms (severe aches and pains, high fever and shaking). If at any point you develop these stop the drug and contact your doctor (GP or Gastroenterologist) as soon as possible.
- Jaundice (rare), Unusual bleeding / bruising (rare), Rashes (rare)
- There are no specific problems for children taking these medicines.
- Lower doses of these drugs may be used in patients aged over 60 years, as there may be a slight increased risk of side effects.
- Avoid driving and hazardous work until you have learned how azathioprine / Mercaptopurine affects you as these drugs occasionally can cause dizziness.
- No known problems with alcohol.
- Theoretically there is an **increased risk of cancer** with Azathioprine. E.g. studies of IBD patients show e.g. a low but significantly increased risk of lymphoma among patients taking thiopurines. The increased risk does not appear to persist after discontinuation of therapy. There may also be an **increased incidence of skin cancers** on Azathioprine.

Special monitoring: Whilst taking this treatment, you will need regular blood tests. Once the dose of treatment is stable, the frequency of blood testing will be reduced (to every 3 months!). The testing will be supervised by your Gastroenterology specialist team or in a shared care arrangement with your GP. These tests include Blood Count (FBC), Liver Function (LFT), Pancreas enzymes. Usually we will also arrange an initial test to measure Thiopurine Methyl Transferase (TPMT) before we start therapy and exclude chronic infections (e.g. Hepatitis B and C, Tuberculosis). FBC and LFT will be checked weekly for four weeks post commencement, then monthly for two months and three monthly thereafter if the results are stable. Any change in dosage will require similar monitoring. You may also be asked to have tests of kidney function from time to time.

Other information:

- Immunisation with **LIVE** vaccines should be avoided. Yearly 'flu' (influenza) and 5 yearly pneumococcal vaccines are safe and should ideally be given to everybody on azathioprine. Please discuss with your General Practitioner.
- Sunscreens and or protective clothing are strongly recommended to reduce sunlight exposure.
- Other medicines that you are prescribed may interact with azathioprine or Mercaptopurine. These include drugs used to treat gout (Allopurinol), the blood thinning treatment warfarin and certain antibiotics (co-trimoxazole and trimethoprim). You should discuss these with your Doctor.

Azathioprine / Mercaptopurine in pregnancy and breast feeding?

Azathioprine is safe to take in pregnancy, although there are reports of premature birth and low birth-weight babies in mothers taking this treatment. Women receiving azathioprine treatment ideally should discuss breast feeding with a specialist. Although Azathioprine is broken down by the body into Mercaptopurine, the use of Mercaptopurine is not recommended during pregnancy. The literature with respect to the safety of thiopurines in men whose partners are planning to conceive is mixed. Data and clinical experience suggest that the drug is safe in this context, although an increased risk of malformations have been reported in other studies.

Note: Mild sickness and headaches are quite common on starting azathioprine (or after an increase in dose). These settle in most people after a few weeks.

Please: Always 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.

This information leaflet is designed to answer common questions patients ask about their medicine. For further information you can contact your Pharmacy, your GP or your Gastroenterology specialist.

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Sources: Medsafe NZ; Falk Pharma Germany; Patient Information NHS UK, British Association of Dermatologists, Clin Gastroenterol Hepatol. 2015 May;13(5):847-58.e4; Risk of lymphoma in patients with inflammatory bowel disease treated with azathioprine and 6-mercaptopurine: a meta-analysis.