NATIONAL ECZEMA SOCIETY

Azathioprine

Introduction

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 in 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' only 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 compared to ciclosporin and benefits are usually not seen until after 4-6 weeks, so it is less suitable for acute flares because it takes longer to take effect. Further improvements then occur over the next few months.

When is azathioprine used?

Azathioprine is mainly used in the UK to treat patients with severe atopic eczema that is unresponsive to normal topical treatment. 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. For patients with normal thiopurine methyltransferase (see opposite), azathioprine can be taken as a single dose. But if side effects such as sickness occur, dividing the dose and taking 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?

Blood tests will be taken before treatment to assess the individual risk for developing side effects. The main problem 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 one 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.

Azathioprine can sometimes cause problems with the liver. Liver function tests are usually checked at the start of treatment and monitored every 3 months – more frequently at the start of treatment. There is also a theoretical concern that long-term treatment may increase the risk of certain types of malignancy but there is no evidence that this is the case in the short-to-medium term. 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, pains and fever.

If this occurs the drug should be stopped immediately and the prescribing doctor informed.

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. In particular, allopurinol – a drug that is used to treat gout – can cause severe bone-marrow suppression. Warfarin (used to thin the blood), and some antibiotics (such a Septrin and trimethoprim) may have a similar effect and should be avoided. Some blood pressure tablets (those that are 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 weekly until a maintenance dose has been established, then blood tests will take place every 3 months.

Can anyone use it?

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

Summary

- Azathioprine is a potent immunosuppressive agent suitable for the treatment of severe, chronic atopic eczema.
- Treatment is started and supervised by consultant dermatologists.
- The main side effects are nausea, altered liver function, 'flu-like' symptoms and the risk of bone-marrow suppression.
- Blood tests are advised before treatment to assess the potential of developing side effects.
- Further blood tests are needed every 3 months during treatment to monitor for any adverse effects.

The National Eczema Society is grateful to Dr Andrew Wright, Consultant Dermatologist, St Luke's Hospital, Bradford, for reviewing and updating this factsheet.

Further information

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