

Azathioprine and 6-Mercaptopurine

This information leaflet aims to answer common questions you may have if you have been given azathioprine or 6-mercaptopurine (6-MP) to treat your Crohn's Disease or Ulcerative Colitis, together known as Inflammatory Bowel Disease (IBD). You can obtain further information from your pharmacist or doctor or from the information leaflet supplied by the manufacturer or from the website: www.medicines.org.uk.

Why have I been started on this medicine?

Azathioprine or 6-MP may be given to you if you keep getting relapses while on initial treatment of IBD, usually aminosalicylates (5-ASAs) and steroids, or if your condition gets worse when steroids are reduced or stopped. They can help you to come off steroid treatment and can be as effective as high dose steroids without causing their side effects. Azathioprine and 6-MP have been found effective in treating up to 7 out of 10 people with IBD. Azathioprine has been used for IBD for more than 30 years and is generally prescribed more frequently than 6-MP. 6-MP is a newer drug which you may be prescribed if you become intolerant of azathioprine.

How do they work?

Azathioprine and 6-MP are chemically closely related and have similar actions. They are types of medicines called immunosuppressants. The immune system is important in fighting infections, but sometimes immune system cells attack the body's own tissues. Azathioprine and 6-MP dampen down the activity of cells in the immune system and reduce inflammation in the bowel. Although the exact mechanism of these immunosuppressants is not known, the way they affect the immune system appears to decrease the activity of IBD.

How long will they take to work?

Azathioprine and 6-MP do not work immediately. It may be 6-12 weeks before you notice any benefit.

When do I take azathioprine or 6-MP?

Once or twice a day after food. You should swallow the tablets whole with a glass of water. If you forget a dose, take it as soon as you remember. If it is almost time for your next dose, do not take the missed dose.

What is the normal dosage?

The dosage of azathioprine varies according to your individual circumstances and your body weight. You will usually start on a low dose which will be increased gradually. The range is typically from 1.5 – 2.5 mg per kilogram of body weight per day. The dose for 6-MP is half that of azathioprine, ranging from 0.75 – 1.5 mg per kilogram of body weight per day.

How long will I be taking azathioprine or 6-MP?

People can usually take azathioprine or 6-MP for up to five years, as long as the blood test monitoring remains satisfactory, and some may take the medication for longer.

What monitoring will I need?

You will need to have regular blood tests the whole time you are taking azathioprine or 6-MP. This is to check that your bone marrow is working properly, as these drugs can suppress normal bone marrow function.

At the start of treatment you will need a Full Blood Count (FBC) and Liver Function Test (LFT), as these drugs can occasionally cause liver problems. You will need blood tests more frequently at the beginning of treatment, usually weekly, then monthly until the maintenance dose is reached and then every 3 months thereafter.

Some centres offer a blood test before treatment to measure an enzyme called TPMT (Thiopurine Methyltransferase). This helps to predict who is more likely to suffer side effects, but as it does not identify all who may be affected, it is more important to be monitored regularly.

Who will do the monitoring?

When you start taking azathioprine or 6-MP your doctor or nurse specialist will explain to you who will manage the monitoring of your medication: it may be managed by your hospital team or shared between your hospital and your GP. You may be given a monitoring booklet to record details of your blood test results. If you have a monitoring booklet you should take it with you every time you see your GP, hospital doctor, pharmacist or nurse, as it helps them to share information.

Will I need to take any special precautions while being treated with azathioprine or 6-MP?

- Try to avoid contact with people who have infections. As azathioprine and 6-MP affect the way the body's immune system works, you may be more prone to infections. You may be at risk of severe infections such as chickenpox or shingles, measles and pneumococcal disease. If you are not already immune you can be vaccinated before starting treatment. Otherwise, tell your doctor or nurse as soon as possible if you come into contact with anyone who has any of these conditions, as you may be able to have a protective injection.
- Avoid driving and hazardous work until you have learned how azathioprine or 6-MP affect you, as these drugs can occasionally cause dizziness.
- Azathioprine and 6-MP increase the skin's sensitivity to sunlight, so you should use sunscreens, and you should avoid sunlamps or sunbeds.
- For those over 60, you may have a slight increased risk of side effects and need to take lower doses.
- There are no special problems for children taking these medicines.

Can I take other medicines along with azathioprine or 6-MP?

Some medicines interact with azathioprine and 6MP. These include allopurinol to treat gout, warfarin, blood thinning treatment, and certain antibiotics, co-trimoxazole and trimethoprim.

You should discuss any new medicines or other preparations, including over-the-counter medicines, herbal, complementary or alternative treatment, with your doctor, nurse specialist or pharmacist before starting them. You should also always tell any other doctor or dentist treating you, that you are taking azathioprine or 6-MP.

Can I have immunisations while on azathioprine or 6-MP?

It may be unsafe to be immunised with certain vaccinations while on azathioprine or 6-MP, which suppress the immune system. You should avoid **live** vaccines such as polio, yellow fever, rubella (German measles), MMR (measles, mumps and rubella) and BCG (tuberculosis). An 'inactivated' polio vaccine can be given instead of the 'live' one. Close relatives and family members may have live vaccines without any risk to you. Pneumovax and yearly flu vaccines are safe and recommended.

Can I drink alcohol while taking azathioprine or 6-MP?

While alcohol is not known to have any interaction with azathioprine or 6-MP, as with any medication, it is better to avoid drinking excessive alcohol.

Does azathioprine or 6-MP affect fertility or pregnancy?

It is important to tell your doctor if you want to start a family or become pregnant, as azathioprine and 6-MP should be used with caution in pregnancy. The evidence is limited about their safety, but research suggests there is more risk if the mother's condition flares up. There are now growing numbers of women who have had successful births while taking an immunosuppressive. For these reasons most doctors advise the continued use of these drugs during pregnancy. You will have to make a balanced decision in discussion with your doctor, based on the risks and benefits.

For men on azathioprine, there is a small amount of evidence for you to stop taking the drug 3 months before starting a family. However this is not conclusive and should be weighed against the risk of a flare-up of your IBD. Men wishing to stop azathioprine should have stable, inactive IBD and should discuss this with their doctor before stopping the drug.

What about breastfeeding?

Breastfeeding is not recommended when taking azathioprine or 6-MP. However, very little of the active drug is secreted into breast milk and there is no evidence of harm in children of mothers on these drugs who have breastfed. For some women the benefits of breastfeeding may outweigh any small potential risk and it is best to discuss this with your doctor.

What are the possible side effects?

All medicines can cause unwanted side effects, which usually improve as your body adjusts to the new medicine. During the early weeks of treatment these drugs can cause nausea, vomiting and loss of appetite, or a flu-like illness with fever and general aches and pains. Taking medication after eating and twice daily instead of all at once may help with nausea. A temporary reduction in dosage may also help, but talk to your doctor or nurse specialist before changing your dose.

These drugs can suppress normal bone marrow function causing anaemia, and a reduction of white blood cells for fighting infection and platelets needed for normal blood clotting. This may lead to weakness or breathlessness, a susceptibility to infections, and a tendency to bruise or bleed easily. Contact your doctor if you develop an infection of any kind.

Occasionally, the drugs may inflame the liver or result in acute abdominal pain due to inflammation of the pancreas (a digestive gland in the abdomen). Or, there may be a sudden worsening of diarrhoea which can be difficult to tell apart from the illness itself. These reactions to the drugs disappear as soon as the drugs are stopped.

There is a slightly increased risk of developing lymphoma (a type of cancer affecting the lymph glands), but a recent extensive analysis of the research concluded that for most

people taking these drugs the risk was very small and the potential benefits outweigh the risk.

There is an increased risk of skin cancer. This should be avoidable with the careful use of sun blocks and avoiding sunbathing and sun lamps.

Other side effects can include dizziness, hair loss and skin rashes.

When should I contact my doctor?

Contact your doctor or IBD nurse specialist in the following situations:

- If you want to change your dose.
- If you have severe side effects.
- If you are going to take any new medication or preparation.
- If you are in contact with anyone who has chickenpox or shingles and you are not already immune.
- If you develop any kind of infection, unusual bruising or bleeding.
- If you want to start a family.
- If you become pregnant.
- If you want to breastfeed.

Who should I talk to if I am worried?

If you are worried about your treatment or if you have any questions, contact your doctor or nurse specialist. You can discuss why it has been prescribed, what the correct dose and frequency is, what monitoring for adverse effects is in place, and what, if any, alternatives are available for you in your particular circumstance.

Where can I get further information?

You can telephone the **NACC Information Line on 0845 130 2233** for further information. You can obtain more information about other drugs used in the treatment of IBD from NACC's booklet *Drugs used in IBD* and from other Drug Treatment Information leaflets. Please call the Information Line for copies or see the NACC website: www.nacc.org.uk to download Drug Treatment Information leaflets.

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We hope that you have found the information helpful and relevant. We welcome any comments from readers, or suggestions for improvements. Please send your comments to Helen Terry at NACC, 4 Beaumont House, St Albans, Herts AL1 5HH – or email h.terry@nacc.org.uk.

The National Association for Colitis and Crohn's Disease (NACC) is a voluntary Association, established in 1979, which has 30,000 members and 70 Groups throughout the United Kingdom.

Membership of the Association costs £12 a year. New members who are on low incomes due to their health or employment circumstances may join at a lower rate. Additional donations to help the work of the Association are always welcomed.