



INFORMATION SHEET

AZATHIOPRINE AND MERCAPTOPURINE

INTRODUCTION

This information sheet is a brief overview of some of the more important points about azathioprine and mercaptopurine for Crohn's Disease or Ulcerative Colitis (UC) (the two main forms of Inflammatory Bowel Disease - IBD). It is about azathioprine and mercaptopurine in general and is not intended to replace specific advice from your doctor or any other health professional. For further information, please talk to your doctor or specialist IBD team or look at the information sheet supplied with your medication, or from the website: www.medicines.org.uk

“

Since moving from rescue therapy to azathioprine, I have got better and better, and been flare-free now for over a year.

”

Paula, age 37

Diagnosed with Ulcerative Colitis in 2014

OTHER NAMES FOR THIS MEDICINE

Both azathioprine and mercaptopurine are produced by a number of manufacturers under different brand names. Azathioprine can be known as Imuran, Azafalk, and Azapress; while mercaptopurine can be known as Puri-nethol. Mercaptopurine is also sometimes called 6-mercaptopurine or 6-MP.

WHY AM I BEING TREATED WITH AZATHIOPRINE AND MERCAPTOPURINE ?

Azathioprine and mercaptopurine are both members of the thiopurine class of drugs and have been used to treat IBD patients since the early 1960s. For Crohn's Disease and Ulcerative Colitis (UC) they are prescribed to around one in five patients to maintain remission (stopping inflammation from coming back) and to help to come off steroids. Mercaptopurine is used less often than azathioprine in the UK. Some patients who cannot tolerate azathioprine (due to side effects) may still be able to take mercaptopurine. Generally IBD patients are not offered thiopurines when first diagnosed, only after they have achieved remission on other treatments. Azathioprine or mercaptopurine are considered as treatment options to help people reduce or stop steroids without suffering another flare-up. These drugs are usually prescribed by IBD specialists, although your treatment may then be monitored by your GP as part of 'shared care'.

HOW DO AZATHIOPRINE AND MERCAPTOPURINE WORK?

Azathioprine and mercaptopurine belong to the group of drugs called immunosuppressants. The immune system is important for fighting infections, but sometimes immune cells attack the body's own tissues and trigger chronic inflammation (like that found in IBD). Azathioprine and mercaptopurine reduce inflammation by damping down over-activity of the cells of the immune system.

HOW EFFECTIVE ARE AZATHIOPRINE AND MERCAPTOPURINE?

A number of studies show thiopurines help maintain remission in both Crohn's Disease and in UC. Research into Crohn's Disease has shown that azathioprine and mercaptopurine can also help bring on remission in active Crohn's, help maintain this remission, and support steroid reduction.

Some studies have suggested thiopurines may prevent flare-ups for people with Crohn's Disease after they have had surgery, although more recent research has shown there is little clear evidence that this is the case. While there is less research looking at the use of thiopurines in UC, studies do show that thiopurines may prevent flare-ups and help maintain remission. Thiopurines are also associated with a lower likelihood of surgery in patients with severe UC treated with ciclosporin (immunosuppressant drug) to bring on remission.

HOW LONG DO THEY TAKE TO WORK?

Azathioprine and mercaptopurine are slow-acting. It may take three to six months before you notice benefits. This means some people will need to be treated with other immunosuppressants, such as steroids, until azathioprine or mercaptopurine have started working.

HOW ARE AZATHIOPRINE AND MERCAPTOPURINE TAKEN?

Both azathioprine and mercaptopurine come in tablet form and are usually taken once a day. The way tablets need to be taken varies according to the drug and its formulation, making it important to take the medicine exactly as your doctor tells you. In general, azathioprine tablets need to be taken with food and swallowed with a glass of water; while azathioprine film-coated tablets and mercaptopurine tablets need to be taken with a glass of water one hour before or three hours after food or milk.

If you forget a dose, take it as soon as you remember, but if it is almost time for your next dose, do **not** take the missed dose. If you take more than you should, go to a hospital straight away taking your medicine packaging with you.

WHAT IS THE NORMAL DOSAGE?

The dose will vary according to your body weight and with the severity of your condition. You may be started on a low dose which is then increased gradually. For azathioprine, the usual dose is between 1.5 mg and 2.5 mg per kilogram of body weight per day. The dose for mercaptopurine is usually half that of azathioprine, ranging from 0.75 – 1.5 mg per kilogram of body weight per day. Doses are also based on the levels of enzymes in your body that break down the drugs (see below **What checks will I need before treatment has started?**) Patients with liver problems and the elderly may need to take lower doses.

HOW LONG WILL I BE TAKING AZATHIOPRINE AND MERCAPTOPURINE?

If you respond well to azathioprine or mercaptopurine, you should be able to keep taking it for some years, provided the results of your monitoring blood tests are satisfactory and you do not develop any serious adverse reactions. Research suggests that the effectiveness of azathioprine and mercaptopurine does not diminish over time. While guidelines state that stopping treatment may be considered after four years for patients remaining in remission, many experts now believe thiopurine treatment should be continued indefinitely. Speak to your doctor if you are considering stopping your treatment.

ARE AZATHIOPRINE AND MERCAPTOPURINE USED IN COMBINATION WITH OTHER DRUG TREATMENTS FOR IBD?

Azathioprine is sometimes given in combination with biological drugs such as infliximab and adalimumab – this is called ‘combination therapy’. Studies in people with Crohn’s Disease and UC have found taking combination therapy with infliximab and azathioprine can be more effective at bringing on and maintaining remission long-term than infliximab alone.

Some people are given azathioprine or mercaptopurine in combination with allopurinol (a drug commonly used for gout). This is because one in five people have high levels of enzymes (proteins that speed up reactions) that convert azathioprine and mercaptopurine to end products that can cause side effects. Allopurinol can correct this imbalance, allowing a slightly larger number of people to tolerate thiopurines. Your doctor will test the level of your enzymes before starting treatment (see below).

WHAT CHECKS WILL I NEED BEFORE TREATMENT HAS STARTED?

- You should have levels of the enzyme thiopurine methyl transferase (TPMT) measured in your blood. This test can help to predict who is more likely to experience side effects with azathioprine or mercaptopurine, such as suppressed bone marrow function. For patients found to have reduced TPMT enzyme levels the dose of thiopurines can be lowered, while those with no detectable levels should be offered alternative treatments.
- You should be screened for immunity to the chickenpox virus and for infections including varicella zoster virus, hepatitis B virus, hepatitis C virus, and human immunodeficiency virus. Screening for Tuberculosis (TB) should also be considered, especially if risk factors are present such as recent visits to countries with high levels of TB, exposure to TB or no previous BCG vaccination for TB.

WHAT CHECKS WILL I NEED DURING TREATMENT?

- You should have regular blood tests for the whole time you are taking azathioprine or mercaptopurine. You will need full blood count (FBC), and liver function tests (LFT), measuring levels of liver enzymes. Both tests are important because azathioprine and mercaptopurine can suppress normal bone marrow function and occasionally cause liver complications. Regular tests are vital as abnormalities in the blood may not produce symptoms straightaway. Recommendations suggest these tests should take place every week for some weeks after starting treatment, then fortnightly until your dose has been stable for six weeks, then monthly and eventually every three months. The frequency of blood tests may vary depending on the hospital that is treating you.
- Kidney function should be monitored every six months.

Treatment monitoring may be managed by your hospital team or shared between the hospital and your GP. You may be given a booklet to record your blood test results that you should take with you every time you see your GP, hospital doctor, specialist nurse or pharmacist, as it helps them to share information.

WILL I NEED TO TAKE ANY SPECIAL PRECAUTIONS WHILE BEING TREATED WITH AZATHIOPRINE AND MERCAPTOPURINE?

- Try to avoid close contact with people who have chickenpox infections. Azathioprine and mercaptopurine affect the way your immune system functions, which can make you more prone to infections. Also, even mild infections, such as a cold or sore throat, may develop into a more serious illness. Contact your doctor if you begin to feel unwell or think you may have caught an infection.
- You may also be more likely to become seriously ill from chickenpox, shingles, measles and pneumonia. If you have not already been vaccinated against these infections, it could be a good idea to do so before starting treatment with azathioprine or mercaptopurine. 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 protective treatment against some of the infections.
- Avoid driving and hazardous work until you have learned how azathioprine or mercaptopurine affects you, as these drugs can occasionally cause dizziness.
- Have regular cervical smears. Research suggests women taking immunosuppressive drugs have increased cervical abnormalities and higher risks of these abnormalities progressing to cervical cancer. Some experts recommend that women who have weakened immune systems should be tested twice during the first year of diagnosis and annually thereafter.
- Azathioprine and mercaptopurine increase the skin's sensitivity to sunlight and the risk of developing some forms of skin cancer. Use sunblock and wear a hat and cover your skin when out in strong sunshine. Do not use sunlamps or sun beds.
- Avoid taking mercaptopurine tablets at the same time as you drink milk. Cow's milk is known to contain high levels of xanthine oxidase, a chemical that inactivates mercaptopurine.

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Being immune suppressed can be a problem. I always make sure I wash my hands thoroughly and with antibacterial soap to try and prevent infection. ”

Jan, age 59

Diagnosed with Ulcerative Colitis in 2011

- Consider carrying or wearing medical alert identification to show you are taking azathioprine or mercaptopurine.

CAN I TAKE ANY OTHER MEDICATIONS WITH AZATHIOPRINE AND MERCAPTOPURINE?

Certain other medicines interact with azathioprine and mercaptopurine. These include allopurinol (so you should not take this unless your doctor has prescribed it to counter side effects – see **Are azathioprine and mercaptopurine used in combination with other drug treatments for IBD?**), warfarin (used to prevent blood clots), 5-aminosalicylates, anti bacterials and febuxostat (used to treat gout). Regular blood test monitoring is needed. If allopurinol is prescribed, the dose of azathioprine will need to be reduced to one quarter to avoid development of neutropenia (reduced levels of white blood cells which help fight infection).

Before you take any new medicines, check with your doctor or IBD team whether there could be an interaction with azathioprine or mercaptopurine. This also applies to any over-the-counter medicines and any herbal, complementary or alternative medicines and treatments. You should also always tell any other doctor, nurse or dentist treating you that you are taking azathioprine or mercaptopurine.

CAN I HAVE IMMUNISATIONS WHILE ON AZATHIOPRINE OR MERCAPTOPURINE?

If you are taking azathioprine or mercaptopurine you should not receive live vaccines, such as polio, yellow fever, BCG (tuberculosis), rubella (German measles) and MMR (measles, mumps and rubella). You should also avoid coming into contact with anyone who has recently received a live vaccine as there is a chance the infection could be passed to you.

New guidelines suggest you should wait at least three weeks from your last immunisation with a live vaccine before starting treatment with azathioprine or mercaptopurine, and you should not have live vaccines until three to six months after stopping treatment.

When first diagnosed with IBD, your doctor should take an immunisation history, and if any gaps are identified, you should be offered 'catch up' vaccinations. Once on thiopurine treatment you will still be able to take inactivated vaccines, such as hepatitis A, and typhoid. Guidelines recommend an annual flu vaccination (with the inactivated vaccine) for people with IBD regardless of whether or not you are taking immunosuppressant drugs. It should be noted that the new nasal spray flu vaccine for children contains live forms of the flu virus and should not be used. Vaccines against pneumonia (such as Pneumovax®) should also be considered.

“

When starting on azathioprine, I made sure I was up-to-date with my vaccinations. I had a pneumonia vaccine and I make sure I have a flu jab every year.

”

Henry, age 27

Diagnosed with Crohn's Disease in 2014

If you are considering vaccinations for travel do talk this through with your IBD team. Sometimes a judgment needs to be made whether the risks of the disease you are being vaccinated against outweigh the risks from live vaccination. It is important not to have any vaccinations during or within six months of stopping thiopurine treatment without consulting your IBD team. See our information sheet: **Travel and IBD** for more details about vaccinations for travel.

CAN I DRINK ALCOHOL WHILE TAKING AZATHIOPRINE AND MERCAPTOPURINE?

Alcohol is not known to have any interaction with azathioprine or mercaptopurine, but for general health reasons it is best to keep within the Department of Health guideline limits. (See **Further Help** for advice on healthy drinking).

DOES AZATHIOPRINE OR MERCAPTOPURINE AFFECT FERTILITY OR PREGNANCY?

Tell your doctor if you are thinking of becoming pregnant or find you are pregnant, and either you or your partner are taking azathioprine or mercaptopurine. Manufacturers' guidelines state azathioprine and mercaptopurine should not be given to patients who are pregnant or likely to become pregnant in the near future. But many experts now feel these drugs can be taken during pregnancy where benefits are judged to outweigh risks. Most doctors recommend women to continue with their azathioprine or mercaptopurine while pregnant as there may be a greater risk to the baby if the woman stops her treatment and as a consequence becomes unwell.

A recent study has shown that mothers taking thiopurines during pregnancy is not associated with low birth weight or birth defects, although links have been made with premature births and anaemia at birth. Long-term studies show children exposed to thiopurines in the uterus have normal mental and physical development and no increased risk of infections.

With regard to fathers taking thiopurines, one study suggests azathioprine and mercaptopurine do not reduce sperm quality, but some manufacturers say mercaptopurine may occasionally cause temporary reductions in sperm counts. However, since active IBD has been associated with abnormal sperm quality, taking medications to maintain remission may help conception.

Older studies reported a slight increase in birth defects in the children of fathers taking thiopurines. However, larger more recent studies have not found this to be the case.

For both men and women, it is important to talk to your IBD team about the risks and benefits for you, so that decisions can be made based on your own individual health.

Regarding contraception, azathioprine and mercaptopurine can reduce effectiveness of intrauterine contraceptive devices (such as the coil) so you might want to consider alternative forms of family planning.

WHAT ABOUT BREASTFEEDING?

If you wish to breastfeed consult your IBD team. The drug manufacturers do not recommend breast feeding by women taking azathioprine or mercaptopurine. However, many experts have suggested that mothers taking thiopurines can breastfeed so long as babies are full-term, healthy and they do not have weakened immune systems. Studies have shown very little active drug is secreted into breast milk and that the drug is not detectable in the babies' blood. There is no evidence of harm in children whose mothers have breastfed while on these drugs.

“

As with any medication, I was apprehensive about side effects. But my symptoms have been very manageable with no flare-ups and very little side effects.

”

Henry, age 27

Diagnosed with Crohn's Disease in 2014

WHAT ARE THE POSSIBLE SIDE EFFECTS?

All medicines can cause unwanted side effects, although not everyone will get them. Estimates suggest side effects occur in around one in five people taking azathioprine and mercaptopurine, and can occur at any time during treatment.

Side effects from azathioprine and mercaptopurine may include the following:

- Nausea (feeling sick), vomiting and loss of appetite. This reaction can be especially strong during the first few weeks of treatment. Taking your medication after eating or in two smaller doses each day instead of all at once as well as reducing dose may help reduce these side effects. Talk to your doctor or nurse specialist before you make any changes to your dose or how you take it.
- In some people, a flu-like illness with fever and general aches and pains a few days or weeks after starting treatment. Tell your doctor if you begin to feel unwell in this way. It is not usually serious but may mean the treatment has to be stopped.
- Suppression of normal bone marrow function, which can cause reductions of red blood cells (anaemia), white blood cells (leucopenia) and platelets (thrombocytopenia). This can lead to weakness, breathlessness and fatigue, a susceptibility to infections, and a tendency to bruise or bleed easily. Regular monitoring should pick up a reduced blood count but it is important that you contact your doctor if you develop an infection of any kind.
- Liver inflammation. Your treatment monitoring will include regular liver function tests (LFTs) to check your liver is working properly. Tell your doctor if you notice a yellowing or discoloration of the skin which may be a sign of jaundice.
- Diarrhoea, which may be difficult to distinguish from symptoms of a flare-up.
- Pancreatitis (inflammation of the pancreas, a digestive gland in the abdomen), which can cause acute pain in the abdomen. Contact your doctor if you experience this type of symptom.
- Uncommon side effects include hypersensitivity reactions where people are allergic to the ingredients of the drugs, and cholestasis (where digestive juice cannot flow out from the liver). Rare side effects include sensitivity to sunlight, hair loss (which in many cases resolves spontaneously despite continuing treatment) and skin rashes.

CAN I RESTART TREATMENT IF I HAVE HAD TO STOP DUE TO SIDE EFFECTS?

For people who have previously stopped treatment due to side effects, revisiting treatment may be possible, with one study suggesting around one in three people can restart treatment. Another study suggests that around seven out of 10 people intolerant of azathioprine can tolerate mercaptopurine.

TELL YOUR DOCTOR IMMEDIATELY IF YOU DEVELOP ANY OF THE FOLLOWING SYMPTOMS

- A sore throat, unexplained bruising, bleeding, or mouth ulcers
- Nausea, vomiting, abdominal discomfort, jaundice or dark urine
- Central acute abdominal pain
- Signs of an allergic reaction including hives (itchy wheals on the skin), difficulty breathing, swelling of the face, lips, tongue or throat.

DOES TAKING THIOPURINES INCREASE THE RISK OF CANCER?

People with IBD treated with thiopurines are at increased risk of cancer due to the drugs making the body's tissues more susceptible and reducing the number of immune cells available to fight cancer. Studies suggest the overall risk of cancer for people taking thiopurines is increased, with the greatest risks for non-melanoma skin cancers (which are generally not life-threatening) and lymphoma (a type of cancer affecting the lymph glands). The skin cancer risk may persist after treatment has stopped so you will always need to use sun protection. However the risk of lymphoma appears to diminish once treatment is stopped. When weighing up these risks of cancer you should bear in mind that research shows no overall increase in mortality among people with IBD exposed to thiopurines.

WHO SHOULD I TALK TO IF I AM WORRIED?

If you are worried about side effects, or have other questions about your azathioprine or mercaptopurine treatment, discuss them with your specialist doctor or IBD nurse. They should be able to help you with queries such as why it has been prescribed for you, what the correct dose and frequency is, what monitoring is in place, what you should do if new symptoms occur, and also what alternatives may be available.

You can find more information about other drugs used in the treatment of IBD from our other Drug Treatment Information leaflets. You can download all our information sheets and booklets for free from our website: www.crohnsandcolitis.org.uk

HELP AND SUPPORT FROM CROHN'S AND COLITIS UK

All our information sheets and booklets are available free from our office and downloadable from our website: www.crohnsandcolitis.org.uk

Crohn's and Colitis UK Information Line: 0300 222 5700, open Monday to Friday, 9 am to 5 pm, except Thursday open 9 am to 1 pm, and excluding English bank holidays. An answer phone and call back service operates outside these hours. You can also contact the service by email info@crohnsandcolitis.org.uk or letter (addressed to our St Albans office). Trained Information Officers provide callers with clear and balanced information on a wide range of issues relating to IBD.

Crohn's and Colitis Support: 0121 737 9931, open Monday to Friday, 1 pm to 3.30 pm and 6.30 pm to 9 pm, excluding English bank holidays. This is a confidential, supportive listening service, which is provided by trained volunteers and is available to anyone affected by IBD. These volunteers are skilled in providing emotional support to anyone who needs a safe place to talk about living with IBD.

FURTHER HELP

NHS Choices

Provide guidance on range of health matters, including alcohol consumption.
Website: www.nhs.uk

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Azathioprine and Mercaptopurine – Edition 4a
Last review: February 2016 - amended May 2016
Next planned review: 2019

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ABOUT CROHN'S & COLITIS UK

We are a **national** charity established in 1979. Our aim is to improve life for anyone affected by Inflammatory Bowel Diseases. We have over 28,000 members and 50 Local groups throughout the UK. Membership starts at £15 per year with concessionary rates for anyone experiencing financial hardship or on a low income.

This publication is available free of charge, but we would not be able to do this without our supporters and members. Please consider making a donation or becoming a member of Crohn's and Colitis UK. To find out how call **01727 734465** or visit www.crohnsandcolitis.org.uk

