



INTRODUCTION

If you've been prescribed azathioprine or mercaptopurine, or are considering it as an option, you're not alone. These medicines are a common treatment for Crohn's and Colitis, with around 6 out of 10 people with the conditions taking them at some point.

Our information can support you to make an informed decision about this treatment that's right for you. It looks at:

- what you can expect from treatment
- how the medicines work
- possible side effects
- stopping or changing treatment.

“

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

”

Paula, age 37
Living with Ulcerative Colitis

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OTHER NAMES FOR THESE MEDICINES

Azathioprine and mercaptopurine are also produced by manufacturers under different brand names.

Azathioprine has brand names Imuran and Azapress.

Mercaptopurine is also sometimes called 6-mercaptopurine or 6-MP.

WHY AM I BEING OFFERED THIS TREATMENT?

Treatment with azathioprine and mercaptopurine aims to:

- prevent flare-ups
- reduce the need to use steroids
- improve your wellbeing by reducing or preventing symptoms including diarrhoea, bleeding and pain.

Azathioprine or mercaptopurine may help you reduce or stop taking steroids without having another flare-up. If you've had two or more flare-ups in 12 months that needed treatment with steroids, or the inflammation in your gut hasn't been controlled by aminosalicylates (5-ASAs) such as mesalazine or sulfasalazine, these medicines could help. Find out more in our information on **Steroids** and **Aminosalicylates (5-ASAs)**.

HOW EFFECTIVE ARE AZATHIOPRINE AND MERCAPTOPURINE?

These medicines don't work for everyone. Your IBD team will talk to you about the other options available if this is the case for you.

Crohn's Disease

Azathioprine and mercaptopurine can help maintain remission in active Crohn's, and reduce the need to use steroids. Some studies have suggested these medicines may also prevent flare-ups for people with Crohn's after surgery.

Ulcerative Colitis

These medicines prevent flare-ups and help maintain remission. Azathioprine may be an effective maintenance treatment for people who can't take tolerate aminosalicylates (5-ASAs) or who need repeated courses of steroids.

HOW DO AZATHIOPRINE AND MERCAPTOPURINE WORK?

Azathioprine and mercaptopurine are immunosuppressants. This means they make your immune system weaker.

The immune system protects us by fighting infections. But in Crohn's and Colitis, the immune system goes wrong and starts fighting the gut instead. This causes inflammation and ulcers in the gut.

Azathioprine and mercaptopurine make the immune system weaker so it can't fight the gut anymore. This reduces the inflammation. However, a weak immune system can mean you're more likely to get infections. Find out more in the section

Will I need to take any special precautions?

HOW LONG DO THEY TAKE TO WORK?

These medicines take some time to work and it may be three to six months before you feel better. You may need to be treated with other immunosuppressants, such as steroids, until azathioprine or mercaptopurine start working.

HOW DO I TAKE AZATHIOPRINE OR MERCAPTOPURINE?

Both azathioprine and mercaptopurine are taken by mouth, usually once a day, and come as 25mg and 50mg tablets.

Azathioprine

You can take azathioprine with a glass of water, with or soon after food - whatever feels better for you. If you find that azathioprine makes you feel sick, or gives you a tummy upset, try taking the medicine after food or at bedtime. It may also help to divide your dose and take it twice a day. Ask your IBD team if you'd like to try this.

It's important to take your medicine in the same way every day to avoid big changes in how the medicine is absorbed.

Mercaptopurine

You can take mercaptopurine with food or on an empty stomach, but it shouldn't be taken with milk or any dairy products. This is because milk contains high levels of an enzyme called xanthine oxidase that stops the medicine working.

Take mercaptopurine tablets one hour before or two hours after you drink milk or eat any dairy products. This includes cream, butter, cheese and yoghurt made with milk from cows, goats or sheep.

It's important to take your medicine in the same way every day.

HOW MUCH SHOULD I TAKE?

The amount you take (the dose) depends on your age, body weight and how active your Crohn's or Colitis is. You may be started on a low dose which is then increased gradually.

Usual doses are:

Azathioprine - between 1.5mg and 2.5mg per kilogram of body weight a day.

Mercaptopurine - between 0.75mg and 1.5mg per kilogram of body weight a day.

Doses are also based on the levels of certain enzymes in your body that break down the medicines. See the section **Do I need any checks before I start treatment?**

Your doctor may alter your dose of azathioprine or mercaptopurine later.

HOW LONG WILL I BE TAKING IT?

If azathioprine or mercaptopurine make you feel better, you should be able to keep taking the medicine for some years. You'll have regular blood tests to make sure this is still right for you.

Stopping treatment may be considered at any time if you don't have any flare-ups. Generally after four years, you and your IBD team will make a decision about whether to continue the medicine. Some people can continue to take the medicine for many years longer. Talk to your IBD team if you would like to think about stopping treatment.

CAN AZATHIOPRINE AND MERCAPTOPYRINE BE USED IN COMBINATION WITH OTHER MEDICINES FOR CROHN'S OR COLITIS?

Biologic medicines

Azathioprine is sometimes given together with biologic medicines such as infliximab or adalimumab. Taking these two different medicines together is known as 'combination therapy'. This can be more effective at bringing on and maintaining remission than taking biologic medicines alone.

This combination may also reduce the likelihood of anti-drug antibodies being produced against these biological medicines, which can reduce how effective they are. But the risk of infection can be higher when azathioprine and biological medicines are used together. See the section on **side effects**.

Allopurinol

Allopurinol is a medicine that is usually used to treat gout, a type of arthritis. But it also changes how azathioprine is broken down and increases the levels of medicine in the bloodstream.

Sometimes when azathioprine is broken down by the body, it can release products that harm the liver. This happens with 1 in 5 people. Your doctor may suggest taking a low dose of azathioprine together with allopurinol, which will boost the levels of azathioprine. This is sometimes known as Low Dose Azathioprine with Allopurinol co-therapy (LDAA).

DO I NEED ANY CHECKS BEFORE I START TREATMENT?

Before you start treatment your IBD team will check that this treatment is right for you.

Blood tests

You'll have blood tests to check your full blood count, liver and kidney function.

- **Levels of the TPMT (thiopurine methyl transferase).** This makes sure the azathioprine doesn't stay in your body for too long. Low levels may mean the azathioprine is building up because it isn't being taken out of your body. This can cause serious side such as suppressed bone marrow function. If you have low TPMT levels the dose of azathioprine or mercaptopurine can be reduced. But if you don't have any detectable TPMT these medicines are not right for you and you'll be offered other treatments.
- **Screening to check that you are immune to specific infections.** Your IBD team may want to check if you've been exposed to a variety of viral infections including HIV, Hepatitis B and C. Having had these infections won't stop you from taking azathioprine or mercaptopurine, but more monitoring may be needed. If you haven't been exposed to chickenpox, you'll be advised to be vaccinated before starting treatment. You may be screened for previous exposure to Epstein Barr virus which causes glandular fever, as people who have never had this virus are at an increased risk of lymphoma.

Vaccinations

You should have all the vaccinations you need before you start treatment. If these are "live" vaccines such as the varicella zoster vaccination for shingles, you'll have this at least two weeks and ideally four weeks before you start azathioprine. See the section **Can I have immunisations while on azathioprine or mercaptopurine?**

DO I NEED ONGOING CHECKS?

When you first start treatment with azathioprine or mercaptopurine you'll need to have regular blood tests. These medicines can reduce normal bone marrow function causing changes in the blood and occasionally liver complications. This may happen over time, so regular tests are important.

Blood tests

Azathioprine affects the way your body produces new blood cells. You'll have regular blood tests for the whole time you're taking azathioprine or mercaptopurine. These will include full blood count and liver function tests.

When you first start treatment, you'll have blood tests every two weeks. Eventually tests are likely to be every three months. But how often blood tests are carried out may vary depending on the hospital that's treating you.

Your IBD team will talk to you if there are any problems and adjust your treatment.

WILL I NEED TO TAKE ANY SPECIAL PRECAUTIONS?

Because azathioprine and mercaptopurine affect the way your immune system works, you may be more likely to get infections. Even a mild infection such as a cold or sore throat could develop into a more serious illness. If you're worried about an infection or an infection is being slow to improve, tell your GP or IBD team.

Reducing the risk of infection

- **Have the annual flu vaccination.** You may also be advised to have a pneumonia vaccination. If left untreated pneumococcal infections can lead to pneumonia (inflammation of tissue in the lungs) septicaemia (a kind of blood poisoning) and meningitis (an infection of the protective membranes that surround the brain and spinal cord).
- **Try to avoid close contact with people who have infections.** This includes viruses and bacteria that cause chickenpox and shingles, measles, and pneumococcal disease. Contact your IBD team or doctor if you begin to feel unwell and think you may have caught an infection.

Reducing the risk of other problems

- **Take care in the sun.** There is a small increased risk of skin cancers for people who take azathioprine or mercaptopurine. So, take precautions in the sun including using a sunblock, wearing a hat and covering your skin when you are out in strong sunshine. Don't use sun beds.
- **Avoid driving and hazardous work until you learn how your medicines affect you.** Azathioprine and mercaptopurine can sometimes cause dizziness.
- **Women should have regular screening for cervical cancer** (previously known as the smear test). There's a small increased risk of contracting the HPV virus that causes cervical cancer if you have Crohn's or Colitis and take these medicines. But there's no need to be tested more frequently than other women, and you'll be invited by your doctor to attend a screening.

CAN I TAKE OTHER MEDICINES?

Before you take any new medicines, check with your doctor, pharmacist or IBD team, because they may interact with azathioprine or mercaptopurine and cause unexpected side effects. This also applies to over-the-counter medicines and herbal, complementary or alternative medicines and treatments.

Some medicines interact with azathioprine and mercaptopurine and include:

- allopurinol (used to treat gout) unless your IBD team has prescribed it
- warfarin (used to prevent blood clots)
- some antibiotics
- febuxat (used to treat gout).

You should also always tell anyone else treating you that you are taking azathioprine or mercaptopurine.

“

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

Living with Ulcerative Colitis

“

When I started 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.

”

Henry, age 27
Living with Crohn's Disease

CAN I HAVE IMMUNISATIONS?

It's not safe to have "live" vaccines while taking these medicines and for three to six months after you stop treatment. Live vaccines contain viruses that have been weakened, but not destroyed. People who are taking medicines which affect the immune system may not be able to produce antibodies quickly enough and risk becoming infected by the disease.

Live vaccines include oral polio, yellow fever, rubella (German measles), BCG (tuberculosis), chickenpox, MMR (measles, mumps and rubella) and shingles. However, you may be able to have the inactivated polio vaccine.

Flu vaccines given by injection are safe. But the children's nasal flu vaccine shouldn't be given as this is live. The Department of Health recommends that everyone on medicines which suppress the immune system should have an annual flu vaccination. But if anyone in your family or household is due to have a live vaccine, check with your IBD team whether you need to take any special precautions.

If you're concerned about the safety of any vaccines or are considering vaccinations for travel, talk this through with your IBD team and see our information on **Travel**.

CAN I DRINK ALCOHOL?

Alcohol isn't known to have any interaction with azathioprine or mercaptopurine.

DOES AZATHIOPRINE OR MERCAPTOPURINE AFFECT FERTILITY OR PREGNANCY?

Tell your doctor if you become or are thinking of becoming pregnant while you or your partner are taking azathioprine or mercaptopurine. For both men and women, it's important to talk to your IBD team about the risks and benefits, so that you can make decisions that are right for you.

Mothers

The companies that make azathioprine and mercaptopurine say the medicines should only be taken when necessary during pregnancy or when trying to conceive, just to be safe. But because the risk is small, many doctors recommend continuing these medicines while you're pregnant. There's more risk to the baby if you stop treatment and become unwell. Studies haven't found any increased risk of miscarriage or birth defects in the baby for women treated with azathioprine or mercaptopurine, compared to women with Crohn's or Colitis who didn't have this treatment when they were pregnant.

But studies have shown increased rates of anaemia (low haemoglobin) in babies born to mothers on these medicines, so a haemoglobin check for the baby may be considered. See our information on **Pregnancy** and **Reproductive Health**.

Fathers

For fathers, taking azathioprine or mercaptopurine hasn't been found to impact the health of the baby and quality of sperm isn't affected.

WHAT ABOUT BREASTFEEDING?

The companies that make azathioprine and mercaptopurine say the medicines should only be taken when necessary during breastfeeding. However, azathioprine and mercaptopurine are generally considered safe for use by breastfeeding mothers. Although a low dose of the drug has been found in breast milk for four hours after taking the medication, so you could consider expressing and discarding milk during this time. Talk to your consultant if you want to breastfeed whilst taking these drugs.

WHAT ARE THE POSSIBLE SIDE EFFECTS?

All medicines can cause unwanted side effects, although not everyone will get them. Side effects occur in around 1 in 3 people taking azathioprine or mercaptopurine, and this can be at any time during treatment. But when considering the risks of side effects, also consider the risks of leaving your Crohn's or Colitis untreated and becoming more unwell.

It's natural to feel concerned when you start taking a new medicine. Our **Helpline** takes many calls on this issue so you're not alone. We can't advise but it may help to talk through your worries.

Immediate reactions.

Any medication can cause an allergic reaction.

Tell your doctor immediately if you develop any of the following symptoms:

- difficulty breathing or swallowing
- rash, hives (swollen red patches of skin) or other signs of allergic reaction
- swollen face including lips and mouth or hands and feet.

Common side effects (experienced by around 1 in 10) people may include the following:

- **Feeling sick (nausea), being sick (vomiting) and loss of appetite.** These reactions can be especially strong during the first few weeks of treatment. Taking your medication after eating or in two smaller doses each day instead may help reduce these side effects. But talk to your IBD team before you make any changes to your dose or how you take it.
- **Flu-like symptoms 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's not usually serious but may mean the treatment needs to be stopped.
- **Diarrhoea.** This may be difficult to distinguish from symptoms of a flare-up.

“

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
Living with Crohn's Disease

Other side effects

Because azathioprine acts on the immune system it can have some more serious side effects. Your IBD team will continue to monitor you to minimise risks but let them know if you:

- think you have an infection including having a fever, sore throat and achiness
- have a bump or open sore which isn't healing
- have yellowing of your skin, feel sick or are sick
- have new warts.
- **Suppression of normal bone marrow function.** This can cause a reduction of red blood cells (anaemia), white blood cells (leucopenia) and platelets (thrombocytopenia). This can lead to weakness, breathlessness and fatigue, being more likely to get 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. Go to Accident and Emergency if you notice a yellowing of your skin or eyes which may be a sign of jaundice.
- **Pancreatitis.** This is inflammation of the pancreas, a digestive gland in the tummy. This can cause severe pain in the centre of the tummy that steadily gets worse then moves to the back. People often also feel very unwell. Usually this occurs within three weeks of starting treatment. Go to Accident and Emergency if you experience this type of symptom.
- **Shingles.** There is an increased risk of shingles (herpes zoster reactivation). If you develop blister-like skin eruptions, you should stop the medication immediately and contact your IBD team. You can normally restart the drug once the rash has healed.

If you're worried about any new or ongoing symptoms talk to your IBD team. The Patient Information Leaflet (PIL) that comes with your medicine also has a full list of side effects. You can also find this at www.medicines.org.uk.

Uncommon side effects (experienced by around 1 in 1000) people may include sensitivity to sunlight, hair loss (which in many cases settles even with continuing treatment) and skin rashes.

DOES TAKING THESE MEDICINES INCREASE THE RISK OF CANCER?

There is a slightly increased risk of some cancers for people treated with azathioprine or mercaptopurine.

Skin cancers

The risk is greatest for non-melanoma skin cancers (which are usually not life-threatening). The skin cancer risk may continue after treatment has stopped so you will need to use sun protection.

Lymphoma (cancer of the lymph glands)

There is a slightly increased risk of lymphoma for people taking azathioprine or mercaptopurine. But this risk is still very small.

AZATHIOPRINE AND MERCAPTOPYRINE

For people with Crohn's or Colitis who don't take azathioprine or mercaptopurine 2 in 10,000 are at risk of lymphoma. For people with Crohn's or Colitis who do take azathioprine 4 in 10,000 are at risk lymphoma.

STOPPING OR CHANGING TREATMENT

There are a few reasons why you and your IBD team might think the time is right for you to stop or change treatment.

Side effects

If side effects develop as they do for around 1 in 3 people, there are a few options. You could try switching from azathioprine to mercaptopurine, reducing the dose or combining a low dose of azathioprine with allopurinol. But if these aren't effective you may need to stop treatment and start on a different type of therapy.

Can I restart treatment if I had to stop due to side effects?

For people who have previously stopped treatment due to side effects, it may be possible to restart after a break. Research suggested that around 1 in 3 people can restart treatment. For people who can't tolerate azathioprine, mercaptopurine can be an option for around 7 out of 10 people.

Long term remission

Stopping treatment may be considered at any point if you're in remission. But most gastroenterologists will usually consider stopping the drug after four years for people who haven't had any flare-ups. However there is a risk of relapsing if you stop taking azathioprine or mercaptopurine. Around 1 in 5 people with Crohn's Disease and 1 in 10 with Ulcerative Colitis are at risk of relapsing within a year of stopping treatment.

WHO SHOULD I TALK TO IF I'M WORRIED?

If you're worried about your treatment or have any questions, talk to your IBD team. They should be able to help you with any queries such as why it's been prescribed, what the correct dose and frequency are, what monitoring is in place, and what alternatives may be available for you.

Your IBD team should give you clear information, talk with you about your options and listen carefully to your views and any worries or concerns you may have. The choice of treatment should be made after talking with your IBD team about the possible advantages and disadvantages of all the options. You can also talk to the Crohn's & Colitis UK **Helpline**.

HELP AND SUPPORT FROM CROHN'S & COLITIS UK

We're here for you whenever you need us. Our award-winning publications on Crohn's and Colitis have the information you need to help you manage your condition.

We have information on a wide range of topics, from individual medicines to coping with symptoms and concerns about relationships, school and employment. We'll help you find answers, access support and take control.

All publications are available to download from our website:
crohnsandcolitis.org.uk/publications

Health professionals can order some publications in bulk by using our online ordering system, available from the webpage above. If you would like a printed copy of a booklet or information sheet, please contact our helpline.

Our helpline is a confidential service providing information and support to anyone affected by Crohn's or Colitis.

Our team can:

- help you understand more about Crohn's and Colitis, diagnosis and treatment options
- provide information to help you live well with your condition
- be there to listen if you need someone to talk to.
- help you understand and access disability benefits.
- help you to find support from others living with the condition.

Call us on **0300 222 5700** or email **helpline@crohnsandcolitis.org.uk**. See our website for LiveChat: **crohnsandcolitis.org.uk/livechat**

Crohn's & Colitis UK Forum

This closed-group community on Facebook is for everyone affected by Crohn's or Colitis. You can share your experiences and receive support from others at: **facebook.com/groups/CCUKforum**

Help with toilet access when out and about

If you become a member of Crohn's & Colitis UK, you will get benefits including a **Can't Wait Card** and a **Radar key** to unlock disabled toilets. This card shows that you have a medical condition and combined with the Radar key will help when you need urgent access to the toilet when you are out and about. See our website for further information: **crohnsandcolitis.org.uk/membership** or call the membership team on **01727 734465**.



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crohnsandcolitis.org.uk and the Information Standard website: www.england.nhs.uk/tis.

We hope that you have found this leaflet helpful and relevant. If you would like more information about the sources of evidence on which it is based, or details of any conflicts of interest, or if you have any comments or suggestions for improvements, please email the Publications Team at publications@crohnsandcolitis.org.uk. You can also write to us at Crohn's & Colitis UK, 1 Bishops Square, Hatfield, Herts, AL10 9NE or contact us through the **Helpline: 0300 222 5700**.

ABOUT CROHN'S & COLITIS UK

We are Crohn's & Colitis UK, a national charity fighting for improved lives today – and a world free from Crohn's and Colitis tomorrow. To improve diagnosis and treatment, and to fund research into a cure; to raise awareness and to give people hope, comfort and confidence to live freer, fuller lives. We're here for everyone affected by Crohn's and Colitis.

This publication is available for free thanks to the generosity of our supporters and members. Find out how you can join the fight against Crohn's and Colitis: call **01727 734465** or visit crohnsandcolitis.org.uk.

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