### Methotrexate

This information is for people with <u>Crohn's</u> or <u>Colitis</u> who are taking methotrexate. It's also for anyone thinking about starting treatment with methotrexate.

Our information can help you decide if methotrexate is right for you. It looks at:

- How methotrexate works
- What you can expect from treatment
- Possible side effects
- Stopping or changing treatment

This information is about methotrexate in general. It should not replace advice from your IBD team.

### **Contents**

Key facts about methotrexate	. 2
Other names for methotrexate	. 3
How methotrexate works	. 3
Why you might be offered methotrexate	. 3
Deciding which medicine to take	. 5
How well does methotrexate work in Crohn's and Colitis?	. 5
How long does methotrexate take to work?	. 7
How to take methotrexate	. 8
Dose of methotrexate	. 8
How long to take methotrexate for	. 9
Taking methotrexate with other Crohn's or Colitis treatments	. 9
Checks before starting methotrexate	10
Ongoing checks	11

Special precautions	11
Side effects	13
Taking other medicines	17
vaccinations	17
Pregnancy and fertility	19
Breastfeeding	19
Drinking alcohol	20
Who to talk to if you are worried	21
Help and support from Crohn's & Colitis UK	21
About Crohn's & Colitis UK	22

### Key facts about methotrexate

- Methotrexate is used to treat Crohn's. Methotrexate is not usually used to treat Colitis.
- Methotrexate is only taken once a week. Never take methotrexate daily.
- It can take up to 12 weeks before you feel the benefits of methotrexate.
- Methotrexate changes the way your immune system works. This means that your body might not be able to fight off infections as well as it used to. Contact your GP or IBD team straight away if you think you have an infection.
- Avoid having live vaccines when taking methotrexate. The annual flu jab and all COVID jabs are non-live vaccines. These are safe to have if you are taking methotrexate.

### **Other names for methotrexate**

The brand name for methotrexate tablets is Maxtrex. The brand names for methotrexate injections include Metoject, Methofill, Zlatal and Nordimet.

### How methotrexate works

When you have Crohn's or Colitis, your immune system does not work properly. Usually, the immune system protects the body against harmful substances and infections. In Crohn's and Colitis, the immune system starts attacking the gut. This causes ulcers and inflammation in the gut.

Methotrexate is a type of medicine called an immunosuppressant. It changes how your immune system works which helps control the inflammation in your gut. Methotrexate does this by stopping your cells from using folic acid to make DNA.

DNA carries genetic information. It has all the instructions that we need to grow, reproduce and function. When a cell is not able to make DNA, the cell will die.

Methotrexate stops immune system cells from replicating. This leads to suppression of the immune system, stopping the attack on your gut.

### Why you might be offered methotrexate

### If you have Crohn's

If you have Crohn's you can have methotrexate both to get the condition into remission and to keep it in remission. Remission means when you have few or no symptoms.

Your IBD team might offer you methotrexate if you can't take other Crohn's treatments such as <u>azathioprine</u>.

Your IBD team might add methotrexate to your treatment if you are taking <u>steroids</u>. This may mean that you can take a lower dose of steroids, as your symptoms will be better controlled. It also means a flare-up is likely to be less severe.

You might take methotrexate along with anti-TNF treatment, such as <u>infliximab</u> or <u>adalimumab</u>. Anti-TNFs are <u>biologic medicines</u>. When you take a biologic medicine, your body can produce antibodies. This can mean that the treatment works less well over time. Methotrexate helps to reduce these antibodies. This means you'll be in remission for longer with biologic treatment.

"I was on methotrexate after a bad experience with azathioprine. It worked for a long time in conjunction with an infusion."

**Zoe** Living with Crohn's

You'll also take **folic acid** tablets when on methotrexate. Folic acid helps reduce some of the possible side effects of methotrexate.

### If you have Colitis

Methotrexate is not recommended for the maintenance treatment of Colitis.

But sometimes people with Colitis may be taking methotrexate. For example:

- To help manage another condition that you may also have, such as rheumatoid arthritis.
- If it is not clear whether you have Crohn's or you have Colitis.
- Alongside some other treatments, to increase the amount of time that you stay in remission.

Your IBD team will be able to give you clear advice on why methotrexate is being recommended to you as a treatment.

### Deciding which medicine to take

There can be a lot of things to think about when you start a new treatment. Your IBD team will discuss the options with you. When considering a new treatment, you might want to think about the potential benefits, possible risks and the goals of your treatment.

Some things to think about include:

- How you will take it.
- How well it works.
- How quickly it is likely to work.
- Side effects you might experience.
- Whether you need ongoing tests or checks.
- Other medicines you are taking.

Our <u>Appointment guide</u> has a list of questions you may want to ask. It can help you focus on what matters most to you. You might find our information about other <u>medicines</u> and <u>surgery</u> helpful.

### How well does methotrexate work in Crohn's and Colitis?

When treating Crohn's or Colitis, the first aim of treatment is to get your symptoms under control. This is induction treatment. Once your symptoms are under control, the aim of treatment is to keep them under control. This is maintenance treatment.

Some clinical trials look at how well a medicine works as induction treatment. Some look at how well it works as maintenance treatment. Some look at how well it works for both.

Find out more about how we talk about the effectiveness of medicines.

#### **Methotrexate in Crohn's**

For Crohn's, we have information about how well methotrexate works for induction treatment and maintenance treatment separately.

#### **Getting Crohn's under control**

These results come from a review that combines the results of several studies. The review compared methotrexate injection 25mg each week with dummy treatment (placebo).

The table below shows how well methotrexate got Crohn's under control after 16 weeks.



#### After 16 weeks of treatment...

After 16 weeks, twice as many people taking methotrexate had their Crohn's under control compared with those who took placebo. About 39% (39 in every 100 people) who took methotrexate had their Crohn's under control compared with 19% (19 in every 100 people) who took placebo.

People who took methotrexate needed less steroids to control their symptoms than those who took placebo. After 16 weeks, the people that took methotrexate needed 50% less steroid dose than those who took placebo.

Methotrexate can be as effective as azathioprine, another treatment for Crohn's. One study compared methotrexate with azathioprine for getting Crohn's under control. It found a similar amount of people in each group had their symptoms under control after 3 months and 6 months. People taking azathioprine had fewer side effects than those taking methotrexate.

#### **Keeping Crohn's under control**

One study compared methotrexate 15mg each week with dummy treatment (placebo) for keeping symptoms under control. The people in the study were already in remission after initial treatment with methotrexate. The table below shows how well methotrexate kept their Crohn's under control after 40 weeks.



After 40 weeks of treatment...

After 40 weeks, more people taking methotrexate had their Crohn's under control than those who took placebo. About 65% (65 in every 100 people) who took methotrexate had their Crohn's under control. About 39% (39 in every 100 people) who took placebo had their Crohn's under control.

Fewer people taking methotrexate needed to take a course of steroids for a flare-up.

### **Methotrexate in Ulcerative Colitis**

In people with Colitis, studies show that methotrexate is similar to placebo for induction and maintenance of remission.

### How long does methotrexate take to work?

Methotrexate will not work straight away. It can take up to 12 weeks before you feel the benefits of methotrexate. Methotrexate injection works more quickly than the tablets.

Keep taking methotrexate even if you do not feel any changes. Taking regular weekly doses is important to treat your condition.

"Don't feel down hearted if you don't see results straight away as it takes time to work."

**Zoe** Living with Crohn's

### How to take methotrexate

Take methotrexate ONCE A WEEK on the same day each week. NEVER take methotrexate daily.

Swallow the tablets with a glass of water. Do not chew or crush the tablets.

If you have methotrexate by injection, a nurse will usually give this to you. These will either be under the skin (subcutaneous) or into the muscle (intra-muscular). Your IBD team may train you on how to give yourself the injection.

If you forget to take your dose of methotrexate, speak to your pharmacist or doctor. You might be able to take the dose up to two days later but should not take it if you are three or more days late. If this happens, take your next dose on your usual day the following week.

### **Dose of methotrexate**

The usual dose of methotrexate for induction treatment is 25mg once a week. You may start on a lower dose and build up to this dose. Once your symptoms are under control, your doctor may lower the dose for maintenance treatment. Doses for children can be lower than this.

If you take methotrexate as tablets, each tablet will usually contain 2.5 mg of methotrexate. You will probably need to take several tablets to make up your dose. For example, if your weekly dose is 15mg, you will take 6 of the 2.5mg tablets.

If you think you may have taken too much methotrexate, go to A&E immediately or contact 999.

#### **Dose of folic acid**

The usual dose of folic acid is 5mg once a week. Some people may need a different dose to help manage the side effects of methotrexate or if they already have a folate deficiency. You should take folic on a different day to your methotrexate. This is because if you take folic acid at the same time as methotrexate, it can stop the methotrexate working so well.

Your IBD team will tell you what dose of folic acid to take and when to take it. Make sure that you know what day you need to take methotrexate and what days you need to take folic acid.

### How long to take methotrexate for

Methotrexate is a long-term medicine. If it works for you, you may need to take methotrexate for months or even years.

### Taking methotrexate with other Crohn's or Colitis treatments

You might take methotrexate at the same time as other treatments for your Crohn's or Colitis. Your IBD team will discuss whether you need to take more than one treatment.

You may take methotrexate along with steroids during induction treatment. The steroid dose will go down once your symptoms are under control.

Methotrexate can also be taken along with anti-TNF treatment, such as <u>adalimumab</u> or <u>infliximab</u>. Giving methotrexate with an anti-TNF can increase the length of time you will be in remission.

### **Checks before starting methotrexate**

Before you start methotrexate, you'll need to have several blood tests to check:

- Liver function.
- Kidney function.
- How healthy your red blood cells and white blood cells are.
- If your liver has hepatitis (inflammation of the liver). A blood test and liver scan will check for this.

Methotrexate can affect your lungs. Your IBD team may check how healthy your lungs are by doing:

- A chest X-ray.
- Lung function tests.

If there is a possibility you might be pregnant, your IBD team may ask you to complete a pregnancy test. This is because methotrexate can harm an unborn baby. See the section on <u>Pregnancy and fertility</u> for more information.

### **Ongoing checks**

While taking methotrexate, your IBD team will regularly check your:

- Liver
- Kidneys
- Red bloods cells and white blood cells

During your appointments, your IBD team may ask if you have:

- Any mouth ulcers
- Unexplained bleeding or bruising
- A sore throat
- A dry cough
- An unexplained rash

When starting treatment, you might have blood tests every 1 to 2 weeks. Once you are stable on the treatment, these blood tests can be every 2 to 3 months.

It's important that you attend your appointments and have regular blood tests. This is to make sure this medicine is working and is safe for you.

### **Special precautions**

Methotrexate can damage your liver. Signs of liver damage include:

- Feeling sick (nausea)
- Being sick (vomiting)
- Dark-coloured pee
- Yellowing of the whites of your eyes or your skin

Speak to your GP or NHS 111 if you have signs of liver damage.

Methotrexate can cause blood disorders. These include low white blood cells (leukopenia), low neutrophils (neutropenia) and low platelets (thrombocytopenia). Having low white blood cells or low neutrophils means you are more likely to get infections. Signs of infection include:

- A sore throat
- A high temperature
- Feeling very tired
- Mouth ulcers
- Muscle aches and pains

Having low platelets means your blood will not be able to clot easily. This means you might bleed or bruise more easily than usual. Keep an eye out for any unexplained bleeding or bruising.

Methotrexate can also affect your lungs. Let your IBD team know immediately if you have any:

- Shortness of breath or trouble breathing
- A dry cough that does not go away
- Chest pain

To be safe, it's a good idea to:

- Attend all routine blood test appointments.
- Be aware of the signs of liver damage, lung damage, infections and bleeding or bruising.
- Know who to contact if you get these signs or symptoms.

Contact your doctor or IBD team immediately if you get any of these symptoms.

Methotrexate treatment may make your skin more sensitive to the sun. Exposure to the sun can cause a severe reaction that looks and feels like sunburn. Exposed skin may develop a rash, redness, swelling, blisters, red bumps or oozing wounds. If the reaction is severe the skin can become infected.

To reduce your risk of a serious reaction to the sun while taking methotrexate:

- Avoid exposure to the sun, especially between 11am and 3pm when the sun is strongest.
- Do not use sun beds or tanning equipment.
- Use sunblock or a sunscreen product with a high protection factor. At least 30 SPF is recommended.
- Wear a hat, and clothes that cover your arms and legs when in the sun.
- If you are worried about a skin reaction, talk to your GP or IBD team.

### Side effects

All medicines can have side effects, but not everyone gets them. Some side effects can happen right away, others might happen later.

Some side effects are mild and may go away on their own or after you stop taking methotrexate. Others may be more serious and could need treatment. Some side effects might mean that methotrexate is not right for you.

Speak to your IBD team if you get any side effects while taking methotrexate.

#### **Possible serious side effects**

#### **Allergic reactions**

Allergic reactions to methotrexate are rare. This means they may affect between 1 in 1000 people to 1 in 10,000 people.

If you think you are having an allergic reaction to methotrexate, speak to your doctor immediately. Go to A&E or contact 999 if you have serious symptoms. Serious allergic reaction symptoms include:

- Difficulty breathing
- Tight chest or tight throat
- Swelling of the face, lips or mouth
- Feeling faint
- A skin rash

#### Infections

Methotrexate can weaken your immune system. This means your body can struggle to fight off infections. Be cautious around other people with infections. This includes chicken pox, shingles and COVID-19.

Contact your GP or NHS 111 immediately if you think you might have an infection. Look out for the signs of an infection, including:

- A fever
- Sore throat
- Dry cough
- Muscle aches
- General flu-like symptoms

#### **Bleeding or bruising**

Methotrexate can lower the platelets in your blood. Platelets help your blood stick together and form a clot when you bleed. When you have low platelets, you are at risk of bleeding or bruising easily.

Contact your doctor or IBD team immediately if you start to bleed without a reason. This includes:

- Bleeding gums
- Blood in your pee or poo
- Abnormal bruises on your body
- Blood in your vomit

#### **Common side effects**

Common side effects can affect between 1 in 10 people to 1 in 100 people. The common side effects of methotrexate include:

- Tiredness
- Headaches
- Diarrhoea
- Feeling sick (nausea)
- Ulcers in the mouth
- Stomach pain
- Losing your appetite
- Heartburn
- Itchy skin or rash

These side effects can be temporary and go away with time. If they cause too much discomfort, speak to your doctor.

#### Less common side effects

Less common side effects can affect less than 1 in 100 people. The less common side effects of methotrexate include:

- Mood changes, such as depression
- Feeling confused
- Dizziness
- Being sick (vomiting)
- Hair loss

If these side effects do not disappear, speak to your IBD team.

This is not a full list of side effects. For more information see the Patient Information Leaflet provided with your medicine. Or visit <u>medicines.org.uk/emc/</u>.

The safety of any new medicine will continue to be monitored after it has become available for use. This is done through longer term clinical studies and reporting of side effects. We encourage you to report any side effects to the Medicines and Healthcare Products Regulatory Agency (MHRA). You can do this through the <u>Yellow Card scheme</u> <u>online</u>. Or by downloading the MHRA Yellow Card app (<u>yellowcard.mhra.gov.uk</u>). This helps collect important safety information about medicines.

> "It's important to speak to your IBD team about any side-effects you are experiencing as they may be able to alter your medication or give you something to help with the side-effects rather than stopping the treatment, as you may find that long term the treatment is very helpful."

#### Alun,

Living with Crohn's

### **Taking other medicines**

Methotrexate can interfere with many different medicines. This includes over the counter remedies and herbal products.

Speak to your doctor or pharmacist if you're taking, or plan to take, any other medicines. This includes medicines you buy from a pharmacy or supermarket, as well as herbal, complementary, or alternative treatments.

Certain medicines should not be taken with methotrexate. These include:

- Some antibiotics, including trimethoprim and co-trimoxazole.
- Anti-inflammatory medicines used for pain relief. These include ibuprofen, diclofenac, naproxen and aspirin. These are normally not recommended for people with Crohn's or Colitis. This is because they may make symptoms worse or trigger a flare-up.

Do not take vitamin or mineral supplements that contain folic acid unless your IBD team has told you to do so.

You can find more information about taking methotrexate with other medicines in the Patient Information Leaflet that comes with your medicine or visit <u>medicines.org.uk/emc/</u>.

Always let your doctor, dentist or pharmacist know you are taking methotrexate. Taking methotrexate can change what treatment you can safely take for other conditions.

### Vaccinations

- You should not have live vaccines until at least 3 months after your last dose of methotrexate.
- If you have had a live vaccine, wait at least 2 to 4 weeks before taking methotrexate.

Live vaccines are made using weakened versions of living viruses or bacteria. If you have a lowered immune system, there is a possibility they might cause infections. Live vaccines used in the UK include:

- TB vaccine.
- Shingles vaccine but a non-live version is also available.
- Chickenpox vaccine.
- Measles, mumps and rubella vaccines.
- Nasal flu vaccine used in children but the injected flu vaccine used in adults is not live.
- Rotavirus vaccine.
- Yellow fever vaccine.
- Oral typhoid vaccine but the injected typhoid vaccine is not live.

If someone you live with is due to have a live vaccine, ask your IBD team whether you need to take any precautions.

The adult flu vaccine is an inactivated vaccine. This is safe to use when taking methotrexate. The nasal flu vaccine used in children contains the weakened live virus. Speak to your child's doctor or IBD team to discuss how they can be protected from the flu.

The annual flu jab and the pneumococcal and COVID-19 vaccines are not live vaccines. They are safe to have while you are taking methotrexate.

If you have Crohn's or Colitis, you are more at risk of getting serious complications if you get the flu. It's important to get your flu vaccine each year when it becomes available.

All types of the <u>COVID-19 vaccine</u> do not contain a live virus. These vaccines are currently recommended if you have a weakened immune system.

Speak to your IBD team if you are unsure about having any vaccines.



### **Pregnancy and fertility**

Do not take methotrexate if you are pregnant.

Methotrexate can harm an unborn baby or cause a miscarriage. Your doctor will make sure you are not pregnant before you start treatment. If you stop methotrexate treatment, try to avoid getting pregnant for 6 months after. This is because the medicine can still be in your blood.

If you could get pregnant, you will be advised to use reliable contraception while taking methotrexate. Methotrexate does not interact with the morning after pill (emergency contraceptive pill) or other contraceptive pills.

Speak to your IBD team if you are planning on becoming pregnant while on methotrexate. They'll help you go through your possible options of treatment. Speak to your specialist if you become pregnant while taking methotrexate.

In the past, men were advised not to try and start a family while taking methotrexate or for 3 months after stopping. There are now several studies that show no increase in harm to babies born where the father was taking methotrexate at conception. Some healthcare professionals still advise waiting for 3 months after you have stopped methotrexate. If your condition is under control and you are worried about stopping treatment, discuss your options with your IBD team.

We have separate information about **<u>Reproductive health</u>** and **<u>Pregnancy and</u>** <u>breastfeeding</u>.

### Breastfeeding

Methotrexate can be present in your breast milk in small amounts. It is not clear if this can harm your baby. Your IBD team or midwife will discuss whether it's safe to take methotrexate when breastfeeding.

Try to avoid breastfeeding for 24 hours after taking a dose of methotrexate. Your baby may need blood tests to make sure the medicine is not affecting them. Speak to your doctor or midwife to find out more.

We have separate information about Pregnancy and breastfeeding.

### **Drinking alcohol**

You can drink alcohol when taking low-dose weekly methotrexate. However, both alcohol and methotrexate can damage your liver. So it is important to stay within the <u>recommended limits</u> (currently 14 units a week).

### Who to talk to if you are worried

Taking medicines and managing side effects can be difficult – we understand and we're here to help. Our Helpline can answer your questions about treatment options and can help you find support from others with the conditions.

Your IBD team are also there to help. You can talk to them about your dose, monitoring and what other options there might be for you. You should also get in touch with your IBD team if you have any new symptoms or side effects.

It can take time to find the medicine that's right for you. Don't be afraid to ask questions and ask for extra support when you need it.

This information is general and does not replace specific advice from your health professional. Talk to your GP or IBD team for information that's specific to you.

### Help and support from Crohn's & Colitis UK

We're here for you whenever you need us. Our award-winning information on Crohn's Disease, Ulcerative Colitis, and other forms of Inflammatory Bowel Disease 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 and employment. We'll help you find answers, access support and take control.

All information is available on our website: crohnsandcolitis.org.uk/information

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.

- Help you understand and access disability benefits.
- Be there to listen if you need someone to talk to.
- 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

Members of Crohn's & Colitis UK get benefits including a Can't Wait Card and a RADAR key to unlock accessible toilets. This card shows that you have a medical condition, and will help when you need urgent access to the toilet when you are out. See <u>crohnsandcolitis.org.uk/membership</u> for more information, or call the Membership Team on 01727 734465.

Crohn's & Colitis UK information is research-based and produced with patients, medical advisers and other professionals. They are prepared as general information and are not intended to replace advice from your own doctor or other professional. We do not endorse any products mentioned.

### 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 information 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 <u>crohnsandcolitis.org.uk</u>.

### **About our information**

Crohn's & Colitis UK information is research-based and produced with patients, medical advisers and other professionals. They are prepared as general information and are not intended to replace advice from your own doctor or other professional. We do not endorse any products mentioned.

We hope that you've found this information helpful. You can email the Knowledge and Information Team at <u>evidence@crohnsandcolitis.org.uk</u> if:

- You have any comments or suggestions for improvements.
- You would like more information about the research on which the information is based.
- You would like details of any conflicts of interest.

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.

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