



INFORMATION SHEET

METHOTREXATE

INTRODUCTION

This information sheet answers common questions about methotrexate as a treatment for Crohn's Disease and Ulcerative Colitis. It is about methotrexate 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 on the website: www.medicines.org.uk.

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METHOTREXATE

OTHER NAMES FOR THIS MEDICINE

Methotrexate is produced by several manufacturers under different brand names, including Maxtrex, Methofill, Metoject, Ebetrex, Namaxir, Nordimet and Zlatal.

WHY AM I BEING TREATED WITH THIS MEDICINE?

If you have Crohn's Disease, methotrexate can help bring on remission, meaning you have few or no symptoms. Methotrexate is less likely to be effective if you have Ulcerative Colitis, but can still be prescribed in some cases.

Your IBD team may suggest you try methotrexate if treatments like aminosalicylates (5-ASAs) and steroids aren't controlling your symptoms, or if you have had a reaction to azathioprine or 6-mercaptopurine. You may also be prescribed methotrexate in combination with biological drugs such as infliximab or adalimumab, to prolong the drug's effectiveness and prevent allergic reactions. You can find out more about combination therapy in our information sheet **Taking Medicines**.

Although methotrexate has been used to treat Crohn's for over 25 years, Inflammatory Bowel Disease is not currently on the list of conditions that methotrexate is licensed for. But it is licensed to treat other conditions, which means the drug has undergone rigorous clinical trials and test to ensure that it is safe. If your doctor thinks that methotrexate will treat your Crohn's or Colitis effectively and the benefits are greater than any risks, then they can still prescribe it for you, even if it is unlicensed.

HOW DOES IT WORK?

Methotrexate belongs to a group of medicines called immunosuppressants. The immune system is important for fighting infections, but sometimes cells in the immune system attack the body's own tissues and trigger inflammation like that found in Crohn's and Colitis. Methotrexate reduces inflammation in the bowel by dampening down over-activity of the immune system. However, this can mean you are more prone to getting infections. For more information see **Will I need to take any special precautions while on methotrexate?**

HOW LONG WILL IT TAKE TO WORK?

Methotrexate does not work immediately. It can take 2 to 3 months before your symptoms improve. Although you may not feel the benefit for some time, it does not mean that the methotrexate is not working. You will be given regular blood tests during this time.

HOW LONG WILL I BE TAKING METHOTREXATE?

If you respond well to methotrexate you will usually remain on it for many months and perhaps several years, providing your blood tests are satisfactory.

“

I sometimes felt sick after taking methotrexate. So I took it on a day I wasn't working, which for me was a Saturday. It meant it had less impact on my work as I was usually feeling less sick by the time I was back at work on Monday.

”

Zoe, age 35

diagnosed with Crohn's Colitis in 2008

WHEN AND HOW DO I TAKE METHOTREXATE?

Methotrexate is taken as a single **ONCE A WEEK** dose on the same day each week. It can be taken in two different ways – either by tablets or by injection. Injections are often the preferred way to take the drug because there is evidence that taking methotrexate by injection is more effective and may cause fewer side effects than tablets when treating Crohn's Disease. (See **How effective and safe is methotrexate?**). Sometimes people start off on the injection form, before moving to oral tablets when the dose is reduced.

- **Tablets:**
Taken by mouth, after food. The tablets should be swallowed whole with a glass of water while sitting upright or standing. Do not crush or chew them.
- **Injection:**
Methotrexate injections can be either subcutaneous (under the skin) or intra-muscular (into muscle). Subcutaneous injections are easier to give and are less uncomfortable. These can be given at the clinic by the nurse, or your nurse may train you to inject the methotrexate yourself.

If you forget to take your methotrexate on your normal day, ask your doctor or pharmacist for advice. You may be able to take it 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. Do not double up your dose.

WHAT IS THE NORMAL DOSAGE?

Doctors and hospitals have different ways of prescribing methotrexate. Some doctors may recommend starting with weekly injections for 8-12 weeks to induce remission, and then moving to weekly oral tablets if it is working well, while other doctors may recommend just the tablet form or the injection form.

For methotrexate injections, the dose advised by NICE (National Institute of Health and Care Excellence) to bring on remission in Crohn's Disease is weekly injections of 25mg. The maintenance dose (to keep you in remission) which is advised by NICE is weekly injections of 15mg.

The methotrexate tablets come in two different strengths: 2.5mg and 10mg. The two strengths are different shapes, but the colour is very similar. It is important that you take the correct strength and dose of tablets. If you think you have the wrong strength, do not use your medicine before checking with your doctor, pharmacist or nurse. Some hospitals and doctors have agreed to use only the 2.5mg tablets to prevent any confusion. Your doctor, pharmacist or nurse will be able to tell you if this applies in your area. If you think you may have taken too much methotrexate, contact your doctor or go to your local Accident and Emergency department immediately.

“

I used to take methotrexate every Wednesday followed by folic acid on a Friday. I never had a problem taking the tablets as they were small and easy to swallow, and I used a weekly pill box so I was less likely to forget taking them.

”

Kelsea, age 28
diagnosed with Crohn's Disease in 2010

“

I was initially given tablets but I couldn't tolerate them. My doctor then prescribed the injections instead, which have been great.

Gemma, age 34
diagnosed with Crohn's Disease in 2014

WHY HAVE I ALSO BEEN PRESCRIBED FOLIC ACID?

Folic acid is a vitamin that can help your body cope with methotrexate and help reduce some of the possible side effects, such as nausea and vomiting. Usually it is taken once a week, but not on the same day as methotrexate. However, a number of different regimes may be used and some people are asked to take folic acid several times a week or every day except the methotrexate day.

HOW EFFECTIVE AND SAFE IS METHOTREXATE?

Methotrexate has been used to treat Crohn's Disease for 25 years. Research has found that a weekly dose of 25mg by injection may bring on remission in Crohn's, while a lower dose of 15mg per week can maintain remission.

There is some evidence that taking methotrexate by injection is more effective and may cause fewer side effects than tablets when treating Crohn's. However, some people prefer to use oral preparations because they are more convenient, and some doctors prescribe the oral tablets to maintain remission once remission has been induced by the injections.

Research on the use of methotrexate for Ulcerative Colitis has shown that it isn't generally effective. Recent studies have shown no benefits of methotrexate for people with Ulcerative Colitis when compared to a placebo (dummy pill).

Sometimes methotrexate is used in combination with anti-TNF drugs such as infliximab or adalimumab. Some studies suggest that methotrexate reduces the risk of developing antibodies to the biological drug. This means that the benefits of the anti-TNF treatment may last longer. It also means the risk of allergic reaction is reduced. But larger trials generally show that there is no improvement when methotrexate is added in combination with an anti-TNF drug.

WILL I NEED ANY SPECIAL CHECKS BEFORE I START TAKING METHOTREXATE?

Before you start treatment you will need to have blood tests, including liver and kidney tests, as methotrexate can affect your blood count and sometimes cause liver problems. Your doctor may also request a chest x-ray, lung function tests, or liver scans. If your bone marrow, liver or kidney function is not working properly, methotrexate may not be suitable for you. If you haven't had chicken pox or shingles, you may be tested to see if you are immune to the virus that causes them, and you may be given a vaccine to protect you from catching the virus before you start taking methotrexate. See **Will I need to take any special precautions while on methotrexate?** and **Can I have immunisations while on methotrexate?**

If you are female, you may be asked to take a pregnancy test before you start taking the drug because methotrexate can be harmful to an unborn baby. See **Does methotrexate affect fertility or pregnancy?**

WILL I NEED ONGOING CHECKS WHILE I AM TAKING METHOTREXATE?

You will need to have regular blood counts and liver tests while you are on methotrexate to check that the treatment is not affecting your blood or liver. A typical approach may be to have blood tests every 1-2 weeks until your condition is stable on the treatment, and then every 2-3 months thereafter. This can show whether you are developing side effects to the methotrexate.

Your 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 test results. Take this with you every time you see your GP, hospital doctor, dentist, specialist nurse or pharmacist, as sharing information helps you to receive safer care.

WILL I NEED TO TAKE ANY SPECIAL PRECAUTIONS WHILE ON METHOTREXATE?

Try to avoid close contact with people with infections. Methotrexate affects the way the body's immune system works, which can make you more prone to infections. Very rarely, a mild infection, such as a cold or sore throat, could develop into a serious illness. Contact your doctor if you begin to feel unwell, have a fever and think you have developed an infection, or are experiencing any other side effects (see **What are the possible side effects?**)

You may also be at greater risk of becoming more seriously ill from the viruses which cause chickenpox and shingles, measles and pneumococcal disease (infection which can lead to pneumonia, blood poisoning or meningitis). If you are not already immune you may be able to 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 for some viruses.

As with all medicines, avoid driving and hazardous work until you have learned how methotrexate affects you, as it can occasionally cause fatigue or confusion.

CAN I TAKE OTHER MEDICINES ALONG WITH METHOTREXATE?

Some medicines interact with methotrexate and could cause unexpected side effects. Always tell your doctor that you are on methotrexate when they are planning to give you any other medication. It is particularly important that you avoid a group of antibiotics called the sulphonamides, which includes co-trimoxazole, and also trimethoprim. You may also need careful monitoring if you take certain other antibiotics.

It is advisable to talk to your doctor or IBD nurse before taking NSAIDs (non-steroidal anti-inflammatory drugs) such as aspirin and ibuprofen because these can interact with methotrexate. These are normally not recommended for people with Crohn's or Colitis anyway because they may make symptoms worse or trigger a flare-up. You should also tell your doctor if you are taking other anti-inflammatory drugs.

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It is also important to tell your doctor, IBD nurse or pharmacist about any other medicines you are taking or thinking of taking, including over-the-counter medicines, such as cold or flu remedies, multi-vitamins, herbal, complementary or alternative therapies.

You should always tell any other doctor or dentist treating you that you are taking methotrexate. It may help to carry a complete list of your medications with you.

CAN I HAVE IMMUNISATIONS WHILE ON METHOTREXATE?

Methotrexate suppresses the immune system. This means that it is unsafe to take certain vaccines and immunosuppressants. You should not receive any of the live vaccines while taking methotrexate, including:

- Polio
- Yellow fever
- BCG (tuberculosis)
- rubella (German measles)
- MMR (measles, mumps and rubella)

However, you can have the 'inactivated' polio vaccine but this may not be as effective.

Yearly flu injections are safe as they are not live vaccines, however, the nasal spray used for children's vaccines is live, and should not be used. It is recommended that people who have long-term health conditions like Crohn's or Colitis have the flu vaccine, regardless of whether you are taking a drug like methotrexate. The pneumococcal vaccine is also recommended for people with a long-term health condition. You may need a single one-off pneumococcal vaccination or a five-yearly vaccination. Speak to your GP surgery or IBD team for further information.

If anyone in your family or household needs to have a live vaccine, such as yellow fever or polio, you should check with your IBD team first. You should also check with your IBD team if you are in contact with a baby or young child on a vaccination programme.

CAN I DRINK ALCOHOL WHILE TAKING METHOTREXATE?

Alcohol and methotrexate can interact and may affect your liver. Your doctor may advise you not to drink any alcohol while you are on methotrexate.

DOES METHOTREXATE AFFECT FERTILITY OR PREGNANCY?

Doctors advise women to use reliable contraception while taking methotrexate. This is because methotrexate can cause birth defects or miscarriages. Also, because traces of methotrexate can remain in body tissue for some time, women are advised to avoid pregnancy for at least 6 months after stopping this drug. Although in the past men were also advised not to try and start a family while taking methotrexate, there are now several studies showing that there is no increase in risk to babies born where the father was taking methotrexate at conception.

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If you find you are pregnant, or decide you would like to have a child while on methotrexate, talk to your doctor about this.

WHAT ABOUT BREASTFEEDING?

There is very little evidence to show the effect of methotrexate on breast milk, but some research shows that the drug passes into breast milk and may affect the baby's immune system and growth. For these reasons you may wish to be cautious and avoid breastfeeding while taking methotrexate. If you have any concerns about this, speak to your doctor or IBD team.

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I was concerned when I was prescribed methotrexate because of the possible side effects. However, it has worked very well for me, and alongside adalimumab has given me a long period of remission after surgery with no obvious side effects.

”

Glenda, age 34
diagnosed with Crohn's Disease in 2012

WHAT ARE THE POSSIBLE SIDE EFFECTS OF TAKING METHOTREXATE?

As with all medicines, methotrexate can cause some unwanted side effects, although not everyone experiences them. Some side effects may be quite mild and go away on their own, while others can be more serious and may require treatment, or may mean that methotrexate is not suitable for you.

The doses used in treating Crohn's Disease are much lower than the doses used for treatments such as chemotherapy for cancer, so the risks of side effects are not as high for people taking methotrexate for Crohn's.

Some of the main side effects and symptoms are described below. (For a full list of side effects, see the Patient Information Leaflet provided with your medication, or visit www.medicines.org.uk.)

Immediate reactions:

- Any medication can cause an **allergic reaction**. For example, sudden wheeziness, feeling faint, having difficulty in breathing, or swelling of the face, lips or mouth.
- **Rash or itching**, especially affecting your whole body.
Common side effects at the beginning of treatment with methotrexate can include **feeling sick, vomiting and diarrhoea**. The following suggestions may help:
 - Taking the folic acid supplement as prescribed
 - Taking your methotrexate at a different time of day, for example before you go to bed at night

If these side effects persist or are severe, talk to your doctor, who may be able to prescribe you an anti-sickness medication to take before your methotrexate. You may also be able to have your dose altered or to switch from the tablet to the injection if you are taking the oral form.

Other side effects:

- As mentioned earlier, methotrexate affects the immune system, and can increase your **risk of infections**, some of which may make you seriously ill. Try to avoid close contact with people who have infections, and contact your doctor immediately if you think you have an infection – this includes having a fever, sore throat and achiness.

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The potential side effects of methotrexate can frighten people, however the benefits of remission outweighed the risk of side effects for me, and I was lucky enough to go into remission on methotrexate.

—
Kelsea, age 28

diagnosed with Crohn's Disease in 2010

”

- In rare cases, methotrexate can **affect the lungs**. Tell your doctor if you become breathless, have a persistent cough, chest pain or difficulty breathing.
- Methotrexate has been known to **damage the liver**. Liver damage may occur with very few outward signs, but in some cases people notice a yellowing or discolouration of the skin or whites of the eyes, or develop severe itching of the skin. If this happens, you should contact your doctor immediately. Regular blood tests can show up liver damage, but special scans and a biopsy of the liver are sometimes necessary.
- Rarely methotrexate can **harm the kidneys**. Kidney function should be checked along with your blood count and liver tests.
- Methotrexate can cause **bone marrow suppression**, which may reduce the number of blood cells made by the bone marrow. It can cause a drop in white blood cells (that fight infection) and platelets (that assist with clotting). If you find that you bruise or bleed easily, have nose bleeds, or have blood spots or rashes on the skin, or have an infection stop taking your methotrexate and contact your doctor immediately. Methotrexate may also cause **anaemia** (lack of oxygen-carrying red blood cells) – your doctor should be able to tell from blood tests whether you have this.
- There is evidence that immunosuppressants such as methotrexate may also slightly increase the risk of **other blood disorders**, such as lymphoma (cancer of the lymph glands). This is why it is important that you continue to have regular blood tests throughout the time you are taking methotrexate.
- Methotrexate can increase the skin's **sensitivity to sunlight**, and the risk of developing some types of skin cancer. This can be reduced by wearing hats, light clothing and high SPF sun block.

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

Seek medical attention if you develop any of these side effects, or notice any other unusual symptoms while on methotrexate.

- Skin rash
- Swelling of the hands, feet, ankles, face, lips, mouth or throat
- Difficulty breathing
- Mouth or gum ulcers
- Hair loss
- Acne
- Abdominal pain
- Vaginal ulceration
- Headache or dizziness or unusual sensations in the head and confusion
- Fatigue or drowsiness
- Blurred vision
- Mobility problems

Overall, it is best to let your doctor or IBD team know about any new symptom you develop while on methotrexate, whenever they occur. Your IBD team should also be able to help with any questions and concerns. Regular blood tests can help to reduce the risk of developing some side effects.

This is not a complete list of side effects of methotrexate, for more information see the Patient Information Leaflet provided with your medication, or visit

www.medicines.org.uk/emc

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WHO SHOULD I TALK TO IF I AM WORRIED?

If you are worried about taking methotrexate or you have any questions about your treatment, contact your doctor or IBD nurse. They should be able to help you with queries such as why it has been prescribed, what the correct dose and frequency is, what monitoring is in place and what alternatives may be available for you.

HELP AND SUPPORT FROM CROHN'S & COLITIS UK

We offer more than 50 publications on many aspects of Crohn's Disease, Ulcerative Colitis and other forms of Inflammatory Bowel Disease. You may be interested in our comprehensive booklets on each disease as well as our other booklets and information covering a variety of topics.

All publications are available to download from:
www.crohnsandcolitis.org.uk/publications. Health professionals can order booklets in bulk by using our bulk ordering system.

If you would like a printed copy of a booklet or information sheet, please contact our Helpline - a confidential service providing information and support to anyone affected by Inflammatory Bowel Disease. Our team can:

- help you understand more about IBD, diagnosis and treatment options
- provide information to help you to live well with your condition
- help you understand and access disability benefits
- be there to listen if you need someone to talk to
- put you in touch with a trained support volunteer who has a personal experience of IBD

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 IBD. You can share your experiences and receive support from others at:
www.facebook.com/groups/CCUKforum

Crohn's & Colitis UK Local Networks

Our Local Networks of volunteers across the UK organise events and provide opportunities to get to know other people in an informal setting, as well as to get involved with educational, awareness-raising and fundraising activities. Visit crohnsandcolitis.org.uk/local-network to find your nearest network.

Help with toilet access

If you become a member of Crohn's & Colitis UK, you will get benefits including a Can't Wait Card and a RADAR key. 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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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**.

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ABOUT CROHN'S & COLITIS UK

We are a national charity established in 1979, fighting for improved lives today and a world free from Crohn's and Colitis tomorrow. We have 40,000 members and 50 Local Networks throughout the UK. Membership costs start from £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 & Colitis UK. To find out how call **01727 734465** or visit crohnsandcolitis.org.uk

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