

Methotrexate

Methotrexate is the 'gold standard' disease modifying anti-rheumatic drug (DMARD) for the control of inflammatory arthritis.

The immune system is overactive in RA and this causes pain, swelling, heat and redness in the joints, stiffness and other symptoms such as fatigue and flu-like symptoms. Methotrexate dampens down this process. This reduces symptoms of RA and the risk of joint damage.

Background

Methotrexate (MTX) was introduced in 1947. At first it was used to treat leukaemia and other forms of cancer.

Starting in the 1980s, methotrexate began to be used to treat adults with RA but in very much lower doses than was used for leukaemia and cancer, after clinical trials had demonstrated its benefits in RA. From the 1990s methotrexate has also been used in children and young people with juvenile idiopathic arthritis.

Research into RA has found that the earlier the treatment starts with a DMARD to control the inflammation, the better the long-term outcome will be.

How does it work?

It has not been possible to identify the way that methotrexate works on the immune system to treat RA.

When used to treat RA, methotrexate must only be taken **ONCE each week**. It should be taken on the same day each week.

It is available as:

- Tablets
- A subcutaneous injection (just under the skin) using a pre-filled pen device
- Oral liquid (suspension)

Your rheumatology team will give you advice on the dose of methotrexate and how to take it. You will also need to take folic acid (one of the B vitamins) to reduce the risk of methotrexate side-effects. Your rheumatology team will also advise on the dose of folic acid and how often it should be taken.

Methotrexate injections (using pens or syringes) need to be kept below 25 degrees centigrade and protected from light, but it doesn't need to go in the fridge.

Most commonly reported side effects

As with any medication, methotrexate can cause side effects. It is important to remember that these are only possible side effects. They may not occur at all.

Side effects may include:

- Feeling sick or being sick (nausea or vomiting), loss of appetite, diarrhoea
- Mouth ulcers, skin rashes
- Blood tests for liver function, white blood cells and platelets may become abnormal

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- Headaches
- Mild hair loss
- Fever, signs of infection, bruising, bleeding
- Skin that is more sensitive to sunlight (photosensitivity)
- Mood swings (these are not very common)

Very rarely methotrexate can cause inflammation in the lungs (pneumonitis). The symptoms of pneumonitis are a troublesome cough and feeling short of breath. This can be very serious, especially if left untreated. If you get these symptoms you should contact your GP surgery or out-of-hours service on the same day

More information on side effects can be found in the patient information leaflet for methotrexate, which will come with your medicine.

Remember to report any concerns about possible side effects to the doctors, pharmacists or nurses.

Methotrexate with other medicines

Folic acid:

Methotrexate can interfere with the absorption of B vitamins, for example folic acid from your diet. Your body needs folic acid to produce new cells, particularly red blood cells.

You will usually be prescribed a folic acid supplement. This will be a much higher dose than folic acid supplements you can buy without a prescription.

Folic acid **MUST NOT** be taken on the same day as methotrexate.

Other medicines:

The antibiotics co-trimoxazole and trimethoprim must **not** be taken when you are taking methotrexate.

You must **not** take high doses of **aspirin** as a painkiller while on methotrexate. Low-dose aspirin (75 to 150mg daily) is safe to take, but higher doses can make it harder for your kidneys to remove methotrexate from your body.

Both methotrexate and **Non-steroidal anti-inflammatory drugs (NSAIDs)** e.g. ibuprofen, naproxen (including those bought without a prescription) can impact the kidneys. Your doctor can advise if it safe and appropriate for you to take both.

Other DMARDs or biologic medications can be prescribed together with methotrexate. These medicines are often used in combination.

Your healthcare team can advise you of any known interactions with your medication, so it is important to let them know about all the medicines you are taking, whether they are prescribed or over-the-counter. You should also let them know if you are taking any supplements or herbal medicines as these can also interact with medicines.

If you start taking any new medicines, check with a doctor, nurse or pharmacist that they are safe to take with any medicines you are currently taking.

Methotrexate and pregnancy

Methotrexate may harm the growing baby and cause birth defects. It is important to not become pregnant when taking methotrexate.

Reliable contraception is important and oral contraceptive (or birth control) pills can be taken with methotrexate. Remember that if you have diarrhoea caused by taking methotrexate your pill may not work.

Methotrexate is believed to be safe to use in males whose partners are trying to conceive when taken at the doses used to treat RA. This is based on limited evidence.

Pregnancy information in this booklet is based on British Society for Rheumatology (BSR) guidelines on prescribing medicines in pregnancy and breastfeeding.

Before starting a family it is recommended that you get advice from the consultant or clinical nurse specialist about trying for a baby and changes to your medicines that may be needed. Generally a woman should wait three to six months from taking their last dose of methotrexate before trying to conceive.

Methotrexate and alcohol

If drinking alcohol, it is important to discuss how to drink safely whilst on methotrexate with the specialist team, as both alcohol and methotrexate are processed in the body by the liver. If the liver is working too hard, this will show up on the liver function tests. The following tips may help:

- Discuss with your rheumatology team about drinking safely, know what the government guidelines are
- Your consultant/clinical nurse specialist will advise you about safe alcohol consumption
- Get an understanding of units of alcohol and recommended daily limits. Visit www.nhs.uk for more information. The size and strength of your drink determines the number of units of alcohol it contains
- The higher the alcohol by volume (ABV) of a drink, the higher the proportion of alcohol it contains. For example, a drink with an ABV of 13 contains 13% pure alcohol
- Limit the amount of alcohol by drinking drinks with a lower alcohol content
- Avoid binge drinking
- Have alcohol-free days
- Avoid having blood tests the day after drinking the night before as this can affect blood monitoring

Methotrexate and immunisation/vaccination

Live vaccines cannot be given to anyone who is already taking methotrexate. The live vaccines used in the UK include: measles, mumps and rubella (MMR), chickenpox, BCG (for tuberculosis), yellow fever, oral typhoid or oral polio (injectable polio and thyroid vaccines can be used). If methotrexate has not yet been started, it is important to seek advice on how long a gap to leave after having a live vaccine.

Annual flu vaccine is strongly recommended. It is available in two forms: an injection for adults and a nasal spray for children. The injectable vaccine is not a live vaccine so is suitable for adults taking methotrexate. The nasal spray is a live vaccine and not suitable for adults taking methotrexate. You can have a flu vaccination at your GP surgery or local pharmacy.

Annual 'Pneumovax' vaccination (which protects against pneumococcal pneumonia) is not live and is strongly recommended. Vaccination with Pneumovax should ideally be given before starting methotrexate.

Shingles (Herpes zoster) vaccine is recommended for all adults turning 65, those aged 70 to 79 and those aged 50 and over with a severely weakened immune system. The vaccination is given as two doses, two months apart. at your GP surgery. It is available as a live or non-live vaccine, so it is important to make sure you are given the non-live version.

Covid-19 vaccines and boosters are not live and are generally recommended for people with RA.

Your GP can advise if you are eligible for free flu, Pneumovax, shingles and Covid vaccinations, depending on the medications you are taking and their doses.

Vaccination of close family members can help to protect someone with a lowered immune system from infection.

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Methotrexate and chickenpox

Around 90% of adults who grew up in the United Kingdom are immune to chickenpox. Before methotrexate is started you may need to have a blood test to check you are immune to chickenpox. If you are not immune, you could be vaccinated against it before starting methotrexate, but this would cause a delay in commencing treatment. Your rheumatology team will discuss with you whether such a delay is acceptable.

Anyone taking methotrexate who comes into contact with chickenpox – and this means being in the same room as someone with chickenpox for 5 minutes or more – should seek advice as soon as possible. They may need to be given antiviral medicines to reduce the risk of serious infection, but need to be assessed by a doctor.

How to reduce methotrexate-related nausea

- Nausea (feeling sick) is one of the common side-effects of methotrexate. Taking methotrexate with your evening meal can make nausea less likely. You should also think about which day is best for you to take methotrexate.
- Folic acid supplements help to prevent many of the possible side-effects of methotrexate.

- Your GP or specialist team may be able to prescribe you anti-nausea medication to help.
- Ginger has been shown to help relieve nausea and can be consumed in many forms, including tea or biscuits.
- Methotrexate injections are less likely to give you nausea than tablets, so you could ask your specialist team if you can switch to injections.

Hints and tips

Prevention of sunburn

Whilst taking methotrexate, your skin may be sensitive to the sun and you may also experience rashes on previously sunburnt skin.

Remember to use sunscreen before going into the sun, as well as a t-shirt and hat and reapply sunscreen frequently as recommended.

Travelling and methotrexate

You may need vaccinations against diseases such as yellow fever, hepatitis A or typhoid depending on where you are travelling to. You

should allow at least a few months to organize this, and must not have live vaccines.

Going by air (flying)

- Inform the airline if you will be carrying methotrexate injections on your flight.
- Methotrexate injections should be carried in your hand luggage, as they might freeze if put in the airplane hold.
- You might also need to get a letter from your healthcare team explaining that you need to take injections in your hand luggage.
- It is a good idea to take a copy of the prescription to show authorities

Methotrexate (MTX) is the gold standard treatment in RA. Many thousands of people are prescribed MTX at diagnosis, so we are regularly contacted by people who are worried about taking it. We therefore felt it was important to list the possible side effects of MTX – and equally important to emphasise that research evidence shows methotrexate to be a safe and effective treatment for many people with RA.

