

Methotrexate factsheet

The immune system plays a vital role in fighting infection, but sometimes, when someone has an autoimmune condition such as eczema, cells of the immune system can attack the body's own tissues and cause inflammation. People with eczema have an impaired skin barrier, which means their skin is drier, so natural moisturising oils leak out and allergens from the environment can enter the skin. This combination triggers the skin's immune-fighting cells to become over-active, causing itching, swelling and the skin becoming red or darker than a person's usual skin colour, depending on skin tone. Methotrexate is an immunosuppressant medicine that dampens down the activity of these immune-system cells to reduce the skin inflammation caused in eczema.

As well as being used to treat eczema, methotrexate has been licensed for many years to treat a number of other inflammatory conditions, including psoriasis and rheumatoid arthritis. It can be used alone or in combination with other treatments. Eczema patients must take this drug only under the supervision of a specialist doctor, such as a dermatologist. It has been used by dermatologists to treat eczema for over 40 years.

How does methotrexate work?

Methotrexate works as an immunosuppressant medication: dampening down overactive inflammatory cells (neutrophils and monocytes), regulating the skin's immune system (T cells), and altering immune signals (cytokines). Methotrexate targets cells of the immune system found in the skin that drive eczema.

It takes several weeks for methotrexate to accumulate inside cells. Therefore, once you start taking methotrexate, it can take up to 12 weeks before you notice any improvement in your skin. It is important that you continue the treatment even if you do not feel any benefit during the first 3-12 weeks (it is likely that the methotrexate is in fact working). Methotrexate usually significantly improves the severity of a person's eczema, enabling them to reduce the amounts of topical treatments used and frequency of application (this does not include emollients, which still need to be applied regularly and liberally). As with any eczema treatment, methotrexate is not a cure.

If your eczema improves with methotrexate therapy, it can be discontinued after a course (often up to a year) or continued on a low dose longer term with appropriate monitoring by your GP and dermatologist.

When is methotrexate used?

Methotrexate is used to treat severe eczema, and is often recommended as a treatment for severe eczema that does not improve with topical steroids, topical calcineurin inhibitors and emollients. This can be because the eczema affects a large area of the body, or because the eczema does not respond sufficiently well to topical treatments alone.

Methotrexate is an effective treatment for severe eczema. In the largest high-quality study of methotrexate for adults with severe eczema, 40 per cent (4 in 10) of patients saw at least a 50 per cent improvement in their eczema after 12 weeks of treatment. Most patients in this study wanted to continue with methotrexate treatment, and after 24 weeks of treatment there was a 50 per cent improvement in the overall eczema severity of the group.

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Methotrexate is taken in tablet or injection form, once a week, on the same day each week. The injection is usually subcutaneous (under the skin) and can be self-administered. Methotrexate is usually started at a low dose, such as 5 mg, once a week (as 2.5 mg tablets). If there are no side effects the dose is then increased weekly to a regular dose of 15-20 mg, once a week (as 2.5 mg and 10 mg tablets). The dose will be adjusted by your dermatologist according to your response to treatment and any side effects.

Methotrexate 2.5 mg and 10 mg tablets look similar, so you should always check the dose of your methotrexate and the strength of the tablets supplied with your dermatologist, nurse and pharmacist. Methotrexate can also be given as a liquid.

If you think you have the wrong strength tablets, do not take the medication. Instead, contact your dermatologist or specialist nurse. Too high a dose can cause serious side effects.

What are the side effects?

It is important to remember that most patients do not experience significant side effects that stop them from taking methotrexate. For those who do experience side effects, these are mostly minor and will improve with time.

The most common side effect of methotrexate is nausea, which usually occurs on the day methotrexate is taken. Your doctor can advise you on how to minimise this, but regular folic acid, anti-sickness tablets and changing from methotrexate tablets to injections can help.

Abnormalities in liver function and blood counts can occur, especially during the first few weeks of methotrexate treatment. For this reason, people taking methotrexate should have regular blood tests, which are more frequent at the start of treatment. These side effects are more common at higher doses, but can occur even in low doses at the start of treatment for some people. Less commonly (fewer than 5%), patients develop mouth ulcers, rashes, diarrhoea and significant abnormalities in blood counts.

Because methotrexate is an immunosuppressant medication and reduces white blood cell count – white blood cells help the body fight infection – people taking it can also be more susceptible to some infections, including chest infections. For patients with eczema, this also sometimes includes viral infections in the skin, such as herpes simplex (the cold sore virus). If you develop chickenpox or shingles while taking methotrexate, you should seek immediate medical attention. You should also have an annual flu jab (see information about other vaccinations on page 4).

Inform your doctor or specialist nurse if you experience a fever, sore throat, any other infection (including infected eczema) or unexplained bleeding/bruising. However, most people notice fewer infections of their eczema while on methotrexate, as their eczema is better controlled.

Methotrexate can cause fibrosis (scarring) of the liver – this side effect is very rare and most likely to occur in patients who are overweight, diabetic, already have liver problems or are taking other drugs that are toxic to the liver. Screening tests undertaken before starting methotrexate help to establish if there are any pre-existing liver problems. While on methotrexate, regular liver blood tests are done to detect any problems with the liver.

Lung problems (persistent cough or unexplained shortness of breath) can also occur (though rarely) when taking methotrexate. These side effects are more common in people with pre-existing poor lung function. Therefore, you should inform your doctor if you experience breathlessness or unexplained breathing difficulties.

Gradual hair-thinning can also affect some patients, but hair usually grows back when the person stops taking methotrexate.

One side effect of methotrexate is to reduce the folic acid in your body. Folic acid is a vitamin, and supplementing it reduces some of the side effects of methotrexate (such as nausea, as mentioned above). You will therefore be given folic acid tablets while you are on methotrexate.

Monitoring your safety

Before you start taking methotrexate, your doctor will do some tests to check that it is safe for you to start treatment. Blood tests will check your blood count, kidney function and liver function. You will also have blood tests for certain viral infections that can become worse on methotrexate treatment (e.g. hepatitis B and C, and HIV). You may also be tested to check that you are immune to the chickenpox virus. If you are not immune to the chickenpox virus, you may be advised to receive a vaccination before starting methotrexate, as this infection can be more serious while taking methotrexate.

Some people will need additional tests before starting methotrexate, such as a chest x-ray or breathing test to check the lungs.

During methotrexate treatment you will need regular blood tests. These tests are to monitor your blood count, kidney function and liver function. Your doctor or specialist nurse will advise you how often blood tests need to be done. When you start taking methotrexate, you will be given a booklet in which the results of your blood tests will be recorded. It is important to keep this booklet up-to-date, and you should take it to any appointments with healthcare providers. It is important that you do not miss your blood tests. You must not take methotrexate unless you are having regular blood tests.

Blood tests are more frequent when you first start taking methotrexate, or when the dose is increased. After you have been taking the same dose of methotrexate for a while, you typically need blood tests once every 2-3 months. If you have an abnormal blood test result, your doctor may tell you to reduce the dose of methotrexate or to stop taking the medication.

If I start to feel unwell or I have a concern, what should I do?

Because methotrexate is an immunosuppressant medication, people taking it can be more susceptible to infection. Therefore, you should inform your doctor or specialist nurse if you experience a fever, sore throat,

any infection (including skin infections, such as herpes simplex) or unexplained bleeding/bruising. Patients who have not had chickenpox or the chickenpox (varicella) vaccination and who come into contact with either chickenpox or shingles should inform their doctor immediately.

If you have any other concerns (e.g. about potential side effects or the dose of methotrexate that you are taking), you should contact your doctor or specialist nurse. Contact details for your doctor or specialist nurse should be in your methotrexate booklet.

Can methotrexate be used with other treatments?

Some medications can interact with methotrexate. These include anti-inflammatory over the counter drugs, such as aspirin and ibuprofen. Paracetamol is generally safe to take. Antibiotics containing trimethoprim must always be avoided.

Before you start taking methotrexate, your doctor will check your other medications. Make sure you tell your doctor about all the medications you are taking. Do not take any over the counter vitamins, supplements or herbal or homeopathic medicines before discussing them with your dermatologist or specialist nurse.

Once you have started taking methotrexate, it is also important that you tell your pharmacist and/or doctor that you are taking methotrexate before any new medication is started, so they can check whether it is safe.

What else do I need to be aware of?

Missing a dose: If you forget to take your methotrexate, do not worry. You can take it on the following day or even the day after that. This will then become the new day of the week to take future doses. Do not take the dose if you are three or more days late. A flare-up of the disease during this time is unlikely.

If you vomit within a few hours of taking methotrexate, contact your doctor or specialist nurse. You may be told

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to take another dose or to wait until the next dose is due the following week. Do not take another dose unless you have been advised to do so by your doctor or nurse.

Methotrexate and alcohol: Medical advice recommends avoiding alcoholic drinks during methotrexate treatment. Methotrexate and alcohol can both cause liver damage. The risk of liver damage from methotrexate is increased by alcohol. Therefore, if you are taking methotrexate, it is best to avoid alcohol altogether. If you still want to drink alcohol, you should limit your intake to well below the recommended limits for safe consumption, which are 2 units per day or 14 units a week for men and women.

Pregnancy and conception: Due to the risk of birth defects, both men and women must avoid conception during methotrexate treatment and for at least 6 months after treatment is stopped. Methotrexate must not be taken in pregnancy. Before starting the medication, a pregnancy test should be undertaken if there is any possibility of your being pregnant. Methotrexate cannot be taken when breastfeeding. Using reliable contraception is critical for both men and women of child-bearing age while on treatment and for 6 months after stopping treatment. Long-term fertility is not affected with this drug.

Planned surgery/dental extraction: Methotrexate can lower your immunity, which can affect wound healing. You should therefore talk to your doctor about whether you should stop using methotrexate if you are about to have surgery or significant dental work.

Vaccinations: Check with your doctor or specialist nurse before receiving any vaccines. If you plan to travel to an area that requires you to be vaccinated, or if you are in contact with a baby or young child undergoing a vaccination programme, ask your doctor or nurse for up-to-date advice.

Covid-19 vaccines available at the time of writing (2021) are safe for people on methotrexate.

The 'live' vaccines such as MMR (measles, mumps, rubella), polio, shingles and yellow fever are no longer contraindicated in people taking methotrexate. This means that you may be able to have these. But the guidelines advise that your suitability for these vaccines should be decided by your doctors on an individual basis. You can check updated vaccine advice for all immunisations at:

<https://www.gov.uk/government/collections/immunisation-against-infectious-disease-the-green-book>

Further information

Additional information can be found in the leaflets inside the tablet packets:

Methotrexate 2.5 mg Tablets

<https://www.medicines.org.uk/emc/product/511>

Methotrexate 10 mg Tablets

<https://www.medicines.org.uk/emc/product/6790>

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