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## Methotrexate

Methotrexate is a successful and popular medicine used for treating severe [psoriasis](#), atopic dermatitis and some other serious or extensive skin conditions. It is also used to treat some forms of arthritis, especially [rheumatoid arthritis](#) and [psoriatic arthritis](#). In much higher doses, it is sometimes used as a chemotherapy agent for leukaemia and some other forms of cancer.

For responding skin diseases, methotrexate usually shows some benefit within 6 to 8 weeks. However, it can cause side effects that occasionally can be serious. Most side effects can be detected before they become serious.

If you are taking methotrexate, please ask your doctor to explain your treatment. Each skin specialist tends to follow a slightly different regime.

### How does it work?

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Methotrexate is now thought to work in skin diseases such as psoriasis and eczema because it has immune suppressive effects. The precise mechanism of action is not understood.

It also reduces the speed in which skin cells proliferate, a particularly useful property in psoriasis because the skin cells are proliferating very quickly. Methotrexate is a folate antagonist – this means it prevents the action of an essential B vitamin, folic acid, on cellular function.

### How to take Methotrexate

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#### **Methotrexate is taken weekly, rather than daily.**

This is different from most medications. The importance of this weekly schedule cannot be overestimated. The weekly dose is taken either as a single or divided dose. Taking methotrexate more often or changing the dose schedule in any way can result in serious side effects.

If doses are taken too often, notify your doctor at once. If an accidental overdose occurs, folinic acid injections may be necessary as antidote and must be given as early as possible.

#### **Other medicines may interfere with methotrexate.**

Many medications may result in an increase in side effects or a decrease in the effectiveness of methotrexate or the other drug. Tell your doctor all the medicines you are taking, whether they are prescription or non-prescription medicines. If you are having an operation with a general anaesthetic, tell the anaesthetist you are on methotrexate.

Do not begin or change the dosage of any medicine without first checking with your doctor. This is especially true of antibiotics and anti-inflammatory agents.

Like methotrexate, antibiotics that contain the drug trimethoprim or cotrimoxazole antagonise folate. Taking them at the same time as methotrexate could result in unexpected and dangerous toxicity.

Aspirin and aspirin-like drugs (nonsteroidal anti-inflammatory medicines) may reduce how much methotrexate is eliminated by the kidneys. This could potentially result in a toxic build-up of methotrexate in the blood stream. Anti-inflammatories can often be taken safely but you should have regular blood tests if you start these medicines or others, as advised by your doctor. Alternatively, you could take paracetamol (acetaminophen), as this does not interfere with methotrexate.

Live vaccines may be ineffective in those taking methotrexate or cause allergic reactions.

### **Illness can increase the risk of methotrexate.**

Dehydration from fever, vomiting, diarrhoea, or decreased fluid intake can be dangerous. Excessive thirst may be a symptom of dehydration. Notify your doctor if these symptoms develop before you take the next dose of methotrexate.

Dehydration or any other reason for reduced kidney function may prevent normal excretion of methotrexate resulting in toxic accumulation of the medication. The excessive methotrexate can in turn damage the kidneys further.

### **Avoid alcohol.**

Alcoholic beverages (including beer and wine) may increase some of the side effects, including the chance of liver damage, and should be severely restricted or avoided altogether.

### **Keep this medicine safely**

Methotrexate should be kept out of the reach of children. Do not give this medication to other people.

## **How should treatment be monitored?**

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Close medical supervision is essential. If you are on methotrexate, to make sure the treatment is safe, it is important that you carry out your doctor's instructions faithfully and promptly report any side effects or symptoms you may develop to him or her.

Blood tests should be arranged to monitor blood count, liver function and kidney function at least. Many centres now offer procollagen tests (P3NP collagen) every 3 to 6 months to see whether liver fibrosis may be occurring.

## **Side effects**

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Side effects can occur at any time during treatment. Regular blood tests (as advised by your doctor, perhaps monthly) and sometimes other types of tests are necessary for the safe use of methotrexate. Your co-operation is essential. A vitamin supplement, folic acid, is thought to reduce some of the side effects of methotrexate without preventing its good effect on the skin disease. Dermatologists often recommend one tablet is taken on several days each week.

If the side effects described below or other problems trouble you, or should you develop any signs of infection or unusual bleeding, notify your doctor promptly and before your next dose of methotrexate is due.

### **Gastrointestinal side effects**

The most common side effects of methotrexate are loss of appetite, nausea (but rarely vomiting), diarrhoea, or sores or ulcers in the mouth. These side effects are usually temporary, but changes in dose may be required, and/or supplemental folic acid tablets. Methotrexate may be unsuitable if you have peptic ulceration or ulcerative colitis. If you have gastroenteritis (stomach upset), do not take methotrexate until you have recovered.

### **Methotrexate must be avoided in pregnancy**

Methotrexate is known to cause birth defects and may cause miscarriage or stillbirth, especially in the first 3 months of pregnancy. Pregnant or breastfeeding women must not take methotrexate, and women of childbearing age must not become pregnant while taking methotrexate. Adequate contraceptive measures are necessary during therapy and for three months thereafter. Consult your doctor before considering pregnancy.

### **Males must take precautions too**

Males should not father children while they are on methotrexate or for at least 3 months afterwards because of its effects on sperm. The risks to the fetus are uncertain.

### **Blood count abnormalities**

An overdose of methotrexate or deficiency of the vitamin folic acid may result in anaemia (decreased haemoglobin count), leucopaenia (reduced white cell count risking serious infections) and thrombocytopenia (low platelet

count resulting in bruising and bleeding). Methotrexate should not be taken unless the blood count is normal or near-normal.

### Liver disease

Methotrexate is stored by the liver. Transaminase liver enzyme levels may rise for a few days after treatment but they quickly return to normal and the next dose may be taken safely.

Long term therapy for two years or more may cause scarring (fibrosis or cirrhosis) of the liver. This is more common in patients with other reasons for liver disease such as viral hepatitis, alcoholism or obesity. Regular blood tests should monitor liver function. Your doctor will look out for persistent transaminase rises and if available, will measure P3NP collagen, which detects liver fibrosis. At times it may be necessary to take a small specimen of liver tissue with a needle (liver biopsy) to determine whether scarring is present. If, and when, to do a liver biopsy should be discussed with your physician.

### Lung disease

Methotrexate can rarely cause a lung reaction similar to pneumonia. The symptoms are usually fever, cough (often dry and hacking), and shortness of breath (which can become severe). Should you develop such symptoms, stop taking methotrexate and notify your doctor promptly. A chest X-ray may reveal diffuse white patches.

### Serious infections

Although uncommon, methotrexate may rarely result in reactivation of tuberculosis or opportunistic bacterial, fungal or viral infections. [Shingles](#) (herpes zoster infection) and [cold sores](#) (herpes simplex) may be more severe in those taking methotrexate.

### Cutaneous side effects

Luckily methotrexate rarely causes skin problems. However, reported effects include:

- Photosensitivity (easy [sunburn](#)): this is uncommon, but it's sensible to cover up and use [sunscreens](#) when outdoors
- Ulceration, particularly in overdose (mouth, lips, skin especially psoriasis plaques)
- Diffuse alopecia (hair loss), uncommon when methotrexate is used for psoriasis but quite frequent in patients receiving larger doses for cancer treatment

Luckily, although classified as a cytotoxic drug, methotrexate appears to have a very low risk of causing cancer even when taken for many years. However, patients with psoriasis do tend to have a higher risk of developing [skin cancer](#) than average, probably because of excessive exposure to the sun and [phototherapy](#). A small increased chance because of methotrexate treatment cannot be ruled out. Skin cancer can usually be treated successfully.

#### Related information

##### On DermNet NZ:

- [Psoriasis](#)
- [Psoriatic arthritis](#)

##### Other websites:

- [Methotrexate injection and tablets data sheet](#) - Medsafe

DermNet does not provide an on-line consultation service.

If you have any concerns with your skin or its treatment, see a [dermatologist](#) for advice.

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