



Australian  
Rheumatology  
Association

# PATIENT INFORMATION ON

# METHOTREXATE

(Brand names: Methoblastin)

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This information sheet has been produced by the Australian Rheumatology Association to help you understand the medicine that has been prescribed for you. It includes important information about:

- How you should take your medicine;
- What are the possible side effects;
- What tests you must have to monitor your condition and to detect unwanted effects; and
- Other precautions you should take.

Please read it carefully and discuss with your doctor.

## What is methotrexate?

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Methotrexate (brand name Methoblastin) is a medicine used to treat rheumatoid arthritis as well as other rheumatic conditions such as juvenile arthritis, lupus, (also known as SLE), psoriatic arthritis and polymyositis (muscle inflammation).

Methotrexate is an immunosuppressive medicine. It works by reducing the activity of several enzymes involved in the immune system. By blocking an enzyme called dihydrofolate reductase, it reduces production of a form of folic acid. It is not entirely clear how methotrexate decreases the severity of arthritis but it reduces inflammation in the joints and associated pain and swelling.

Because methotrexate reduces the damage to the joints, rather than just relieving the pain, it belongs to the group of medicines called **disease modifying antirheumatic drugs (DMARDs)**.

Methotrexate has been used to treat rheumatoid arthritis for more than twenty years.

It is also used at very high doses (1000mg-5000mg a day) to treat some cancers.

For more information about RHEUMATOID ARTHRITIS see the Arthritis Australia website [www.arthritisaustralia.com.au/index.php/arthritis-information/information-sheets.html](http://www.arthritisaustralia.com.au/index.php/arthritis-information/information-sheets.html).

## What benefit can you expect from your treatment?

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Methotrexate is one of the most effective treatments for rheumatoid arthritis. Most, but not all, patients will benefit from this medicine. Some achieve remission, where the arthritis virtually disappears.

Methotrexate does not work straight away. Reduced pain, stiffness and swelling may be noticed after 4 weeks. The effects to delay or prevent joint damage will take several months.

Other medicines may be given to improve your symptoms while waiting for methotrexate to work.

## How is methotrexate taken?

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Methotrexate may be taken by mouth as a tablet or given by injection either into the muscle or under the skin.

Injections may be used instead of tablets if the medicine is not being absorbed well, or if you feel sick (nausea) or vomit when you take the tablets, or your condition is not improving with tablets.

### ***When should it be taken?***

Methotrexate is taken just **once a week**, on the same day each week. If you are taking the tablets, it is a good idea to specify and diarise the day of the week that you will take your tablets to avoid making mistakes.

If you take the tablets at night on an empty stomach you will absorb them best. Taking the medicine in the evening or at meal time may also help to reduce nausea.

### ***What is the dosage?***

Tablets come in 2.5mg or 10mg strengths. Treatment usually starts with a very low dose, which is increased and adjusted depending on the response, up to about 25mg once a week.

The dose is usually taken all at once on a single day. It may be divided into separate doses taken during that day if necessary.

### ***Are other medicines taken with methotrexate?***

Folic acid or folinic acid are recommended while you are taking methotrexate as they reduce the risk of side effects. Your doctor will explain how much of the folic/folinic acid to take and when to take it.

Methotrexate is often taken in combination with other arthritis medicines, including:

- other DMARDs;
- biological DMARDs (a newer type of DMARD, which act on natural substances in the body that contribute to inflammation and joint damage);
- steroid medicines such as prednisolone or cortisone injections into the joint;
- anti-inflammatory medicines (NSAIDs) such as naproxen (Naprosyn) or ibuprofen (Brufen/Nurofen); and/or
- simple pain medicines such as paracetamol.

### ***How long is the treatment continued?***

The treatment is continued indefinitely as long as it is effective and as long as no serious side effects occur.

If methotrexate treatment is stopped for more than a few weeks there is a risk that your condition may worsen. Continue with your treatment unless advised by your doctor or unless side effects develop.

If you have an illness, which makes you unwell enough to change plans for the day, e.g. gastroenteritis or fever, it is reasonable to miss the weekly dose until you have recovered.

### **Are there any possible side effects?**

Below are side effects that you might experience with your treatment. Tell your doctor if you experience any side effects.

If you do experience side effects, a reduction in dose may minimise these so that you can continue to take the medicine. Your doctor will advise on any dose changes that are necessary.

### **Most common possible side effects:**

- The most common side effects are *nausea*, *vomiting* and *diarrhoea*. These can be reduced if methotrexate is taken with food or in the evening. Antinausea tablets can be used if needed.
- *Mouth ulcers* can occur, but the use of folic acid or folinic acid supplements makes this less likely.
- *Skin dryness, a variety of skin rashes and increased sensitivity to the sun* may also occur. You should wear sunscreen and a hat when out in the sun.
- Some people report mild *tiredness*, *headache* and *mental clouding*. Some also experience a temporary increase in muscle and joint pain after taking the weekly dose.

### **Less common or rare possible side effects:**

There are some rare but potentially serious side effects with methotrexate.

- **Blood counts:** Methotrexate can rarely cause a drop in the number of white blood cells, which are needed to fight infection. It can also cause a drop in the number of platelets, which help to stop bleeding. Regular blood tests aim to pick these problems up early if they occur. However, if you develop a sore mouth, mouth ulcers, easy bruising, nosebleeds, bleeding gums, breathlessness, infection or fever tell your doctor straight away.
- **Liver:** Methotrexate can inflame the liver causing a type of hepatitis. Regular blood tests aim to pick this up early if it occurs.

The dose of methotrexate may need to be reduced or stopped if problems occur. Liver problems may be increased when methotrexate is combined with the medicines azathioprine (Azahexal, Imuran,) or leflunomide (Arava), or with heavy alcohol use (see *Alcohol* overleaf).

- **Lungs:** Methotrexate can cause inflammation of the lungs. This is more likely if leflunomide also being taken. This may develop quickly. If you have a sudden onset of breathing difficulties seek medical attention as soon as possible. The problem may also develop slowly with symptoms such as a dry cough.
- **Hair thinning:** This may occur rarely. It is not permanent and hair will grow back when the medicine is stopped.
- **Cancer:** see below.

### Long term possible side effects:

Methotrexate may be taken for long periods e.g. more than twenty years, to manage rheumatoid arthritis. In addition to **possible effects** mentioned above, the following are rare but possible long term side effects, or long term issues that may concern patients:

- **Liver:** Very rare cases of increased fibrous tissue in the liver have been reported after long term treatment. Regular monitoring can minimise the risk of this occurring.
- **Cancer:** People who have rheumatoid arthritis have an increased risk of lymphoma (a lymph node cancer). It is not clear whether methotrexate increases this risk further, but any additional risk is likely to be very small. Methotrexate may reduce the risk of these cancers by controlling the rheumatoid arthritis, but this is unproven. For general cancer prevention, stopping smoking is recommended. An annual skin check to detect any early skin cancer is also recommended.
- **Fertility:** Methotrexate **does not** affect a person's ability to have children in the long term. See also *Precautions* overleaf.

### More information about possible side effects

Information that comes with your methotrexate medicine will also outline in detail potential serious side effects that may

occur with methotrexate. Many of those side effects relate to **high dose** methotrexate for the treatment of cancer. These may not be applicable to the much lower doses that are prescribed for the treatment of rheumatoid arthritis. Talk to your doctor if you have concerns about any possible side effects.

## What precautions are necessary?

### *Blood tests:*

- As methotrexate may affect the liver and blood cells, you **must** have regular blood tests during your treatment. This is very important, as you may not get symptoms with some of these problems.
- Blood tests are particularly important during the first few months of treatment and when methotrexate is taken with leflunomide.
- As well as monitoring for side effects, blood tests help to monitor your condition to determine if the treatment is effective.
- You will need to have full blood counts and liver function tests every 2 to 4 weeks for the first few months of treatment and then every 1 to 3 months after that.
- If there are no problems seen after 3 months of treatment at a specific dose of methotrexate, the blood tests may be done less frequently.
- Your general practitioner will be informed about the monitoring schedule. It is important to see them if you have been asked to do so as they play an important role in monitoring your condition.

### *Avoid infections:*

- Because your immune system may be depressed, there is an increased risk of developing some infections, especially herpes zoster (chicken pox and shingles). You should try to avoid contact with people who have these infections. If you have an infection or persistent fever, tell your doctor straight away.

### *Other medicines:*

- Methotrexate can interact with other medicines. You should tell your doctor (including your general practitioner, rheumatologist and others) about all

medicines you are taking or plan to take. This includes over the counter or herbal/naturopathic medicines. You should also mention your treatment when you see other health professionals.

- Antibiotics containing trimethoprim (e.g. Bactrim, Septrim or Triprim) can cause problems when taken with methotrexate and should be avoided.
- Aspirin can be used safely in the low doses taken for prevention of heart attack and stroke.
- Methotrexate can be taken safely with anti-inflammatory drugs (NSAIDs), as long as your kidney function is normal.
- The simple pain reliever paracetamol, and combined medicines such as Panadeine and Panadeine Forte, can be used while taking methotrexate provided you take them as directed.
- Most vaccines can be given safely. Pneumovax and yearly flu vaccinations are safe and recommended to reduce your risk of those infections. Talk with your rheumatologist before receiving any vaccines.

**Alcohol:**

- Alcohol increases the risk of liver damage while taking methotrexate. Methotrexate usage in heavy drinkers has been associated with cirrhosis of the liver.

- It is not known precisely what level of drinking is safe when on methotrexate, however there is general agreement that 1-2 standard drinks taken once or twice a week is unlikely to cause a problem.
- Drinking more than 4 standard drinks on one occasion, even if infrequently, is strongly discouraged.

**Surgery:**

If low dose once weekly methotrexate is continued during surgery, there seems to be no change in wound healing or increased infection.

**Pregnancy and breastfeeding:**

- Methotrexate should not be taken during pregnancy as it can cause miscarriage or foetal deformity. It should also not be taken during breastfeeding.
- Women of child bearing age should use effective contraception while taking methotrexate.
- Women planning to become pregnant should stop methotrexate 3 months before attempting to conceive.
- The optimal time for a male partner to stop methotrexate before trying to conceive is not known.
- Methotrexate does not affect a person's ability to have children in the long term.

**All patients taking methotrexate should be seen regularly by a rheumatologist to optimise treatment and to minimise any potential side effects. You must have regular blood test when taking this medicine. Failure to do so will increase your risk of side effects.**

**If you have any questions or concerns write them down and discuss them with your doctor.**

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**Your doctor's contact details:**

**REMEMBER – Keep all medicines out of reach of children**

The information in this sheet has been obtained from various sources and has been reviewed by the Australian Rheumatology Association. It is intended as an educational aid and does not cover all possible uses, actions, precautions, side effects, or interactions of the medicines mentioned. This information is not intended as medical advice for individual problems nor for making an individual assessment of the risks and benefits of taking a particular medicine. It can be reproduced in its entirety but cannot be altered without permission from the ARA.

The NHMRC publication: *How to present the evidence for consumers: preparation of consumer publications* (2000) was used as a guide in developing this publication.