

# *Professor Roger K A Allen*

## Methotrexate and Sarcoidosis

### Information for Patients

(adapted from the Australian Rheumatology Association patient information handout)

Methotrexate (brand names Ledertrexate® and Methoblastin®) is a medicine used to treat rheumatoid arthritis as well as other rheumatic conditions, such as systemic lupus erythematosus (SLE/lupus) psoriatic arthritis and polymyositis (muscle inflammation). It is also very useful for sarcoidosis and has been used for at least 30 years.

Methotrexate is used at very high doses (1000 mg – 5000 mg a day) to treat some cancers.

Methotrexate is an immunosuppressive medicine, which means that it works by reducing the activity of the immune system by acting on folic acid metabolism. In rheumatoid arthritis, this action helps to reduce inflammation and thus reduce pain and swelling. It also limits damage to the joints and helps to prevent disability in the long term.

Because Methotrexate reduces the damage to the joints, rather than just relieving the pain, it belongs to the group of medicines called disease-modifying anti-rheumatic drugs (DMARDs). However, its action in sarcoidosis is more widespread than just affecting joints.

#### ***What benefit can you expect from your treatment?***

Methotrexate is one of the most effective treatments for rheumatoid arthritis and sarcoidosis. Most, but not all, patients will benefit from this medicine.

Methotrexate does not work straight away. An improvement in sarcoidosis may be noticed after four weeks, especially with skin involvement.

Other medications such as corticosteroids and hydroxychloroquine (Plaquenil) may be given to improve your symptoms while waiting for methotrexate to work.

#### ***How is Methotrexate taken?***

Methotrexate may be taken by mouth in tablet form.

#### ***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.

It is a good idea to take the tablets with food to minimise nausea (feeling sick) and vomiting. Taking the medicine in the evening may also help to reduce nausea.

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

Tablets come in 2.5 mg or 10 mg strengths. Treatment usually starts with a very low dose, which is increased and adjusted depending on the response, up to about 20 mg 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.

### ***Always double check the dose the pharmacist dispenses***

Folic acid should be taken every day in a dose prescribed (usually 0.5 mg/day). Don't buy over the counter folic acid.

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

To minimise side-effects, folate supplements should be taken while you are on methotrexate.

Methotrexate is often taken in combination with other arthritis medications.

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

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

If methotrexate treatment is stopped for more than a few weeks, there is a risk that your condition will get worse again. 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 side-effects?***

Below are the 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 side-effects:**

- The most common side-effects are *nausea (feeling sick)*, *vomiting* and *diarrhoea*. These can be reduced if methotrexate is taken with food or in the evening. Anti-nausea tablets can be used if needed.
- *Mouth ulcers* can occur, but the use of folic acid supplements makes this less likely.

- *Skin dryness*, a variety of *skin rashes* and *increased sensitivity to the sun* may also occur. It is a good idea to 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 side-effects:**

- *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 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 have to be reduced or stopped if problems occur. Liver problems may be increased when methotrexate is combined with azathioprine or leflunomide. Very rare cases of increased fibrous tissue in the liver (called cirrhosis) have been reported after long-term treatment. Regular monitoring can minimise this.
- *Lungs*: methotrexate may cause inflammation of the lungs. This may develop slowly, with symptoms such as dry cough. It may also develop quickly with a sudden onset of breathing difficulties.
- *Hair thinning*: This may occur rarely. It is not permanent and hair will grow back when the medicine is stopped.
- *Cancer*: People who have rheumatoid arthritis have an increased risk of lymphoma (a lymph node cancer). There is no such increased risk in sarcoidosis. It is not clear whether methotrexate increases this risk further, but any additional risk is likely to be very small. Methotrexate may in fact reduce the risk of these cancers by controlling the rheumatoid arthritis, but this is also unproven.

The 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 outlined related to the use of **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.

#### **What precautions are necessary?**

##### *Blood tests:*

Since the liver and blood cells may be affected by methotrexate, you must have regular blood tests during your treatment. This is very important, as you may not get symptoms with some of these problems.

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 two to four weeks for the first few months of treatment and then every one to three months after that.

If there are no problems seen after three 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 your general practitioner if you have been asked to do so as they have an important role to play 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 about all medicines you are taking or plan to take. This includes over the counter or herbal/naturopathic medications. You should also mention your treatment when you see other health professionals.

Certain antibiotics (Septrim or Triprim, which are sulpha drugs) 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 attacks 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 but live vaccines, such as measles vaccine, should not be given while you are taking methotrexate.

#### *Alcohol:*

Because methotrexate can affect the liver, you should avoid heavy alcohol use while taking it.

#### *Pregnancy and breastfeeding:*

Methotrexate should not be taken during pregnancy or during breastfeeding.

If you are a woman of childbearing age, you should use effective contraception while taking methotrexate. It is also recommended that men do not take methotrexate when they are trying to conceive.

Methotrexate does not affect a person's ability to have children in the long term.