

## **METHOTREXATE**

### **What is Methotrexate?**

Methotrexate is one of the most effective and commonly used medications in the treatment of rheumatoid arthritis and other forms of inflammatory arthritis, and also may be used to treat lupus, inflammatory myositis, vasculitis, and some forms of childhood arthritis. It is often used in combination with other medications to treat arthritis. It is known as a disease-modifying anti-rheumatic drug (DMARD), because it decreases the pain and swelling of arthritis, and also decreases damage to joints and long-term disability.

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

Methotrexate comes either as tablets or as a subcutaneous injection. Methotrexate is usually taken as a single dose once a week on the same day of each week. Occasionally the dose is split into two doses, taken on the same day, to improve absorption or to avoid side effects. Methotrexate tablets are best taken on an empty stomach. However, if nausea is a problem, taking them at meal time can help reduce the side effect without much loss of benefits. If you forget to take a dose, it can be taken the next day or the day after. If your dose is more than 2 days late, contact your dose for advice. Never take 2 doses together. If you have an illness for e.g. gastroenteritis or fever, it is reasonable to omit the weekly dose until you have recovered. Folic acid (or folate) is prescribed with the methotrexate to decrease the chance of side effects. The folate should be taken the day after methotrexate. Improvements in arthritis and other conditions usually are first seen in 3 - 6 weeks. The full benefit of this drug may not be seen until after 12 weeks of treatment.

### **What are the side effects?**

Most Common:

(Folic or Folinic acid helps to reduce side-effects)

Fatigue, nausea, vomiting or 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/sores

Less common/Rare:

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

Skin dryness, a variety of skin rashes and increased sensitivity to the sun.

Blood counts: Methotrexate may cause a drop in the number of white blood cells, which can lower your immune system's ability to fight infections. It can also cause a drop in the number of platelets and haemoglobin.

Regular blood tests aim to pick these problems up early if they occur.

If you develop a sore mouth, persistent sore throat, fever or other signs of infection, mouth ulcers, easy bruising, nosebleeds, bleeding gums, breathlessness – tell your doctor straight away.

Hair loss: It is not permanent and hair will grow back when the medicine is stopped. It can be managed by taking folic acid.

Liver: Methotrexate can inflame the liver and this can be seen on blood testing. 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 other liver toxic drugs or with heavy alcohol use.

Lungs: Methotrexate can cause inflammation of the lungs. This may be more likely if leflunomide is being taken at the same time. The problem may develop quickly, so if you have a sudden onset of breathing difficulties seek medical attention as soon as possible. It may also develop with symptoms such as a dry cough.

Nodule formations: Methotrexate can increase nodule formation in patients with rheumatoid arthritis.

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**Long term:**

Methotrexate may be taken for long periods (> 25 yrs.). The following are rare but possible long-term issues:

**Liver:** Very rarely methotrexate may cause liver cirrhosis. This risk is increased when combined with alcohol. Regular monitoring can minimize the risk of this occurring.

**Cancer:** People who have rheumatoid arthritis and other similar inflammatory conditions 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 also reduce the risk of these cancers by controlling the inflammation. 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.

### **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.

You will need to have full blood counts and liver function tests, as determined by your doctor.

**Risk of infections:**

Because your immune system may be depressed, there is an increased risk of developing some infections, especially Herpes zoster (chicken pox and shingles).

If you develop symptoms of an infection, you should stop methotrexate and contact your doctor.

#### Use with other medicines:

Antibiotics containing trimethoprim (e.g. Bactrim, Septrim or Triprim) can cause problems when taken with methotrexate.

Most vaccines can be given safely. Current recommendations are that low dose methotrexate (0,4 mg/kg per week) is not a contraindication to live vaccines, such as Zostavax, MMR (measles, mumps and rubella), oral polio or yellow fever but such live vaccines should be avoided at higher doses of methotrexate.

Discuss any vaccinations with your rheumatologist.

Pneumovax and yearly flu vaccinations are safe and recommended to reduce your risk of those infections.

#### Use with 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 to 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.

#### Use in pregnancy and breastfeeding:

Methotrexate should not be taken during pregnancy as it can cause miscarriage or foetal deformity. It should also not be taken when breastfeeding. Women of child-bearing age should use effective contraception.