



## Methotrexate (*Rheumatrex, Trexall*)

### Description

Methotrexate (*Rheumatrex*) is one of the most effective and commonly used medicines in the treatment of several forms of arthritis and other rheumatic conditions. It is known as a disease-modifying anti-rheumatic drug (DMARD), because it not only decreases the pain and swelling of arthritis, but it also can decrease damage to joints and long-term disability.

### Fast Facts

- Methotrexate is one of the most commonly used drugs in the treatment of rheumatoid arthritis.
- It helps with pain and swelling and also slows the progression of arthritis over time.
- Methotrexate requires careful monitoring to reduce risk of liver injury and infections.
- Methotrexate can cause serious birth defects and should not be taken while breastfeeding.

### Uses

Methotrexate has been used for decades to treat psoriasis and some cancers. It is used to treat 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.

### How it works

Methotrexate blocks several enzymes involved in the immune system. This affects actively growing cells such as those that are in the skin, blood, gastrointestinal tissues (i.e., stomach and intestines), and the immune system. However, it is not entirely clear how methotrexate decreases the severity of arthritis.

### Dosing

Methotrexate comes in 2.5 milligram (mg) tablets. Adults with rheumatoid arthritis usually begin with a starting dose of 7.5 to 10 mg, or 3-4 pills, taken all together once a week. The dose may be increased to 20 to 25 mg a week over time if needed. The medication also can be given as a liquid or as an injection. This comes as 25 mg per 1 milliliter (mL) and is injected under the skin, like insulin, to reduce side effects or when higher



doses are needed. Adults with other rheumatic conditions may take similar doses. In children with juvenile arthritis, the dose is based on the patient's weight.

### **Time to effect**

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.

### **Side Effects**

The most common side effects of methotrexate include nausea or vomiting and abnormalities in liver function tests. Liver function tests are blood tests your doctor may order to watch your liver. These side effects are more likely to occur at higher doses. About 1-3% of patients develop mouth sores (called stomatitis), rash, diarrhea, and abnormalities in blood counts. Methotrexate may cause cirrhosis (scarring) of the liver, but this side effect is rare and most likely to occur in patients who already have liver problems or are taking other drugs that are toxic to the liver.

Lung problems (persistent cough or unexplained shortness of breath) can occur when taking methotrexate. These side effects are more common in people with poor lung function. Persistent cough or shortness of breath should be reported to your doctor.

Slow hair loss is seen in some patients, but hair grows back when the person stops taking this medication. Methotrexate can increase the sensitivity of the skin to sunlight, so limiting sun exposure and the use of sunscreen is advised.

The use of folate supplements (folic and folinic acid) often are given with methotrexate. These are B vitamins and can decrease side effects during methotrexate treatment.

It is important to remember that most patients do not experience side effects, and that, for those who do, many of the minor side effects will improve with time. Methotrexate treatment should be discontinued for at least three months before attempting to become pregnant. Even though methotrexate should not be taken during pregnancy, it does not reduce a woman's chance of becoming pregnant in the future.

### **Points to remember**

Methotrexate should not be taken if you are pregnant or plan to become pregnant, or if kidney or liver function is not normal.

It is important to take methotrexate exactly as directed. Generally, this medication should be taken one day a week, but the dose is occasionally split into two doses per week to avoid side effects. Your doctor also may prescribe a folic acid (folate) vitamin supplement to decrease the chance of side effects. Some side effects do not cause symptoms, so it is important to have routine blood tests performed every 8-12 weeks.

If you miss a dose, you can generally take it up to 4-5 days later. If you do not realize that you missed a dose until the next dose is scheduled, talk to your doctor about what to do. If you are about to have surgery, talk to your doctor about whether or not to discontinue methotrexate. When methotrexate treatment is discontinued, its beneficial effects on arthritis symptoms gradually disappear over a period of 2-8 weeks.



Alcohol significantly increases the risk for liver damage while taking methotrexate, so alcohol should be avoided while on this medication.

**Methotrexate can cause serious birth defects and complications during pregnancy, so it is important that you discuss birth control and pregnancy plans with your physician while taking this medication.** An effective form of contraception is critical while taking methotrexate and for at least three months after stopping the medication. Some vaccinations should be avoided while taking this medication. Be sure to discuss with your doctor before receiving any vaccines. Also, be sure to notify your doctor before any surgeries while taking this medication.

### Drug interactions

Be sure to tell your doctor about all of the medications you are taking, including over-the-counter drugs and natural remedies, as some of these could increase the risk of methotrexate toxicity. Trimethoprim (*Bactrim*), an antibiotic used for respiratory and urinary infections, may increase the toxicity of methotrexate. The level of methotrexate can be affected by nonsteroidal anti-inflammatory drugs (NSAIDs), although these often are prescribed together for the management of rheumatoid arthritis. Other drugs that can affect the liver may increase the risk of liver damage from methotrexate. Radiation therapy, used to treat some cancers, may increase the risk of serious side effects from methotrexate.

### Information to Discuss with Your Primary Care Physician and other Specialists

Be sure to tell your other physicians that you are taking this drug. Women taking this medication should discuss appropriate forms of birth control with their primary care physician or gynecologist. It is especially important that women discuss the use of this medicine (even past use) with their obstetrician/gynecologist. Live vaccines should be avoided while on this medication. You should discuss updating your vaccinations prior to starting this medication. Because this medication can lower your immunity, it is important that you discuss this with any physician treating you for an infection, as this may lead to a different evaluation or treatment. The risk of liver injury may be increased if methotrexate is combined with other medications. Be sure to discuss this with other physicians when new medications are prescribed.

### For more information

The American College of Rheumatology has compiled this list to give you a starting point for your own additional research. The ACR does not endorse or maintain these Web sites, and is not responsible for any information or claims provided on them. It is always best to talk with your rheumatologist for more information and before making any decisions about your care.

National Institutes of Health: Medline Plus Link

<http://www.nlm.nih.gov/medlineplus/druginfo/meds/a600032.html>

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Written by Michael Cannon, MD, and reviewed by the American College of Rheumatology Patient Education Task Force.

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