

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

^{Pr}**Methotrexate Injection USP** (meth-o-TREX-ate)

Read this carefully before you start taking **Methotrexate Injection USP** and each time you get an injection. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **Methotrexate Injection USP**.

Serious Warnings and Precautions

- Methotrexate Injection USP should be prescribed by a healthcare professional who is experienced with the use of methotrexate.
- Methotrexate Injection USP dosage forms that contain benzyl alcohol as a preservative must not be used:
 - for intrathecal (into the spinal canal/fluid) or intracerebroventricular (into the cavities of the brain) infusions.
 - for high-dose treatment.
 - in newborn babies less than one month old.
- Methotrexate Injection USP can cause serious side effects that may result in death.
- **Pregnancy and breastfeeding - Female patients:**
 - Methotrexate Injection USP can harm your unborn baby, cause birth defects or cause you to lose the pregnancy.
 - Do not use Methotrexate Injection USP if you are pregnant, think you are pregnant or are planning to get pregnant during or after your treatment. If you want to get pregnant, talk to your healthcare professional.
 - If you are able to get pregnant, you:
 - will have a pregnancy test done before starting Methotrexate Injection USP. The result of this test must be negative. Pregnancy tests may be repeated during your treatment, especially if you miss using your birth control.
 - must use effective birth control during your treatment and for 6 months to 1 year after your last dose.
 - Avoid becoming pregnant while you are using Methotrexate Injection USP.
 - Tell your healthcare professional right away if you get pregnant or think you are pregnant during your treatment.
 - Methotrexate Injection USP passes into breastmilk. Do not breastfeed while you are using Methotrexate Injection USP. If you are currently breastfeeding, stop before you start Methotrexate Injection USP.
- **Pregnancy - Male patients:**
 - Do not father a child while you are using Methotrexate Injection USP.
 - Use effective birth control during your treatment and for at least 6 months to 1 year after your last dose. Female sexual partners should also use effective birth control.
 - If, during your treatment, your female sexual partner becomes pregnant or thinks she may be pregnant, tell your healthcare professional right away.
 - You should not donate sperm during treatment for at least 6 months to 1 year after your last dose.

What is Methotrexate Injection USP used for?

Methotrexate Injection USP is used in high doses to treat certain types of cancers, including breast cancer, Non-Hodgkin's lymphoma and leukemia.

Methotrexate Injection USP is used at lower doses to treat adults with the severe disabling conditions listed below when other treatments do not work. This means the conditions prevent the patient from carrying out their regular activities.

- Rheumatoid arthritis (joint inflammation caused by the immune system)
- Psoriasis (a chronic skin disease)
- Psoriatic arthritis (a kind of joint inflammation that affects people with psoriasis)
- Ankylosing spondylitis (inflammation in the joints and ligaments of the spine)
- Reactive arthritis (inflammation that can happen after another illness)
- Enteropathic arthritis (arthritis that happens in people who have inflammatory bowel disease, IBD)

How does Methotrexate Injection USP work?

Methotrexate Injection USP works by blocking an enzyme process in cancer cells so that they cannot grow. Methotrexate Injection USP also reduces the activity of the immune system (the body's own defence mechanism). It is used to modify and slow the worsening of psoriasis, rheumatoid arthritis and other disabling conditions. It will not cure them. Some normal cells in the body may be affected as well.

What are the ingredients in Methotrexate Injection USP?

Medicinal ingredients: methotrexate (as methotrexate sodium)

Non-medicinal ingredients: benzyl alcohol (as preservative), hydrochloric acid, sodium chloride, sodium hydroxide and water for injection

Methotrexate Injection USP comes in the following dosage forms:

Sterile solution:

10 mg / mL

20 mg / 2 mL (no preservative) as a single-use vial

25 mg / mL

50 mg / 2 mL (no preservative) as a single-use vial

50 mg / 2 mL (with preservative) as a multidose vial

500 mg / 20 mL (with preservative) as a multidose vial

Do not use Methotrexate Injection USP if:

- you are allergic to methotrexate, any of the non-medicinal ingredients, or any component of the container (see **What are the ingredients in Methotrexate for Injection, USP?**)
- you have severe kidney problems, kidney failure, or are on dialysis
- you are sexually-active, pregnant or planning to get pregnant. Both male and female patients must use effective birth control methods all the time while taking Methotrexate Injection USP and for a few months after the last dose.
- you are breastfeeding
- you have psoriasis or rheumatoid arthritis and the following:
 - suffer from alcoholism (drink excessive alcohol), or alcoholic liver disease or other severe liver disease
 - your immune system does not work as well as it should (immunodeficiency)

- blood or bone marrow problems:
 - low level of cells in the bone marrow (bone marrow hypoplasia)
 - low level of platelets (thrombocytopenia)
 - low red blood cells (anemia)
 - low white blood cells (neutropenia, leukopenia)
- you are going to receive a general anesthetic called nitrous oxide. It is also known as laughing gas.

Methotrexate Injection USP dosage forms that contain benzyl alcohol as a preservative must not be used:

- for intrathecal (into the spinal canal/fluid) or intracerebroventricular (into the cavities of the brain) infusions.
- for high-dose treatment.
- in newborn babies less than one month old.

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take Methotrexate Injection USP. Talk about any health conditions or problems you may have, including if you:

- have kidney problems. Your healthcare professional may want you to drink extra fluids so that you will have more urine to pass. This will help Methotrexate Injection USP to pass from your body.
- are dehydrated or experience a lot of vomiting, diarrhea, or sweating
- have or have had liver problems, including hepatitis B or hepatitis C infection
- have lung problems
- have problems with your immune system, or active infections
- have problems with your bone marrow
- have previously had radiation treatment to a large area of your body
- have gastrointestinal problems such as mouth sores or inflammation, peptic ulcer disease or ulcerative colitis (inflammatory bowel disease)
- have skin problems
- have a neurologic disorder
- drink alcohol
- have previously been treated with cisplatin
- have aciduria, a condition where urine becomes acidic
- are experiencing weakness (debility)
- have fluid on your lungs (pleural effusion) or in your abdomen (ascites)
- are over 65 years of age. This is because side effects may be more likely.
- recently received or are going to receive a vaccine
- are obese
- have diabetes

Other warnings you should know about:

Sun and UV light exposure: Some patients who use Methotrexate Injection USP may become more sensitive to sunlight than they normally are. Avoid too much sun exposure and do not use a sunlamp until you see how you react to the sun, especially if you tend to burn easily. If you have been treated with radiation before, you may develop a reaction rash or sunburn to that area while using Methotrexate Injection USP. As well, your psoriasis sores can become worse if you are exposed to UV-rays during your treatment.

Serious blood and bone marrow problems: Methotrexate Injection USP can cause blood and bone marrow problems, which can increase your chance of getting infections and affect how your blood clots, which may lead to bleeding. To reduce the risk of infection or bleeding, you should:

- Avoid people with infections. Check with your healthcare professional right away if you think you are getting an infection or if you get a fever or chills, cough or hoarseness, lower back or side pain, or painful or difficult urination.
- Avoid anyone who has had the oral polio vaccine for at least 6 weeks. Do not get close to them or stay in the same room as them for very long. If this is not possible, wear a mask over your nose and mouth.
- Check with your healthcare professional right away if you notice any abnormal bleeding or bruising; black, tarry stools; blood in urine or stools; or red spots on your skin.
- Be careful when using a regular toothbrush, dental floss, or toothpick. Check with your healthcare professional before having any dental work done.
- Do not touch your eyes or the inside of your nose unless you have just washed your hands.
- Be careful not to cut yourself when you are using sharp objects such as scissors or a razor.
- Avoid contact sports or other situations where bruising or injury can happen.

Serious lung problems: Methotrexate Injection USP can cause sudden bleeding in the lungs. This is called **Pulmonary alveolar haemorrhage**. If you suddenly spit or cough up blood you must go to the hospital right away. You will need emergency care. This occurs in patients with some existing health problems. Some examples are rheumatic disorder (pain in your joints) or vasculitis (swelling in an artery or vein).

Progressive Multifocal Leukoencephalopathy (PML): Methotrexate Injection USP can cause a rare brain infection called PML.

Driving and operating machines: Methotrexate Injection USP can cause fatigue and dizziness. Before you drive or do tasks that require special attention, wait until you know how you respond to this medicine.

Fertility: Methotrexate Injection USP may affect your ability to have a child in the future (fertility).

- Females may have abnormal periods or have no period at all. Methotrexate Injection USP can affect egg production.
- Males may have a low sperm count. The sperm may also have changes in their DNA.
- These changes can happen during treatment and for a short period after your last dose.

Check-ups and testing: You will have regular visits with your healthcare professional before, during and at the end of your treatment. They will do blood and urine tests to check your liver and kidney health, do liver biopsies, lung tests and/or chest x-rays. Your healthcare professional will decide when to do these tests and will interpret the results.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

Serious Drug Interactions

Do not take Methotrexate Injection USP if you are going to receive a general anesthetic called nitrous oxide. It is also known as laughing gas.

The following may interact with Methotrexate Injection USP:

- medicines to reduce pain, fever or inflammation called Non-steroidal anti-inflammatory drugs (NSAIDs), including acetylsalicylic acid (ASA), phenylbutazone and other pain killers
- certain Disease Modifying Antirheumatic drugs (DMARDs), such as gold taken by mouth or injection, penicillamine, hydroxychloroquine, sulfasalazine, leflunomide, azathioprine
- phenytoin, a medicine used to treat seizures
- probenecid, a medicine used to treat gout
- medicines used to treat bacterial and fungal infections including penicillins, tetracycline, vancomycin, nystatin, neomycin, trimethoprim/ sulfamethoxazole, ciprofloxacin, pristinamycin, chloramphenicol, amphotericin B, kanamycin, polymyxin B, sulfonamides
- theophylline, a medicine used to treat asthma
- the vitamin folic acid or vitamin preparations that contain folic acid
- medicines used to treat cancer including cytarabine, mercaptopurine, L-asparaginase, folinic acid and radiation therapy
- medicines used to treat acid related stomach problems called proton pump inhibitors (PPIs) including omeprazole, esomeprazole, and pantoprazole
- pyrimethamine, a medicine used to treat parasitic infections
- amiodarone, a medicine used to treat irregular heart beat
- medicines used to treat diabetes called sulfonylureas
- packed red blood cells, used for blood transfusions
- Psoralen Plus Ultraviolet Light (PUVA) therapy, a type of ultraviolet light treatment for severe skin conditions
- medicines called diuretics or “water pills” used to lower blood pressure and decrease swelling including triamterene
- some vaccines
- azathioprine, a medicine used to prevent transplant organ rejection
- aminobenzoic acid, a medicine used to treat Peyronie’s disease
- medicines used to treat acne called retinoids

Do not drink alcohol during your treatment with Methotrexate Injection USP. Alcohol can increase the chance of liver problems.

Tell any healthcare professional that is treating you that you are taking Methotrexate Injection USP.

How to take Methotrexate Injection USP:

Methotrexate Injection USP will be given to you by a healthcare professional in a healthcare setting.

- Do not take more or less of it, and do not take it more often than your healthcare professional has prescribed. The exact amount of medicine you need has been carefully worked out. Taking too much may increase the chance of side effects, while taking too little may not improve your condition.
- In most cases, Methotrexate Injection USP is taken once weekly on the same day of the week.
- In some cases, your healthcare professional may tell you to take Methotrexate Injection USP every 12 hours for 3 doses. You should only do this once a week. Do not take more than 3 doses each week.
- Methotrexate Injection USP should never be taken every day of the week when used to treat psoriasis, rheumatoid arthritis or in most cases of cancer.

- Taking Methotrexate Injection USP daily, or in a dose larger than prescribed can result in serious side effects, often requiring hospitalization, and sometimes resulting in death. Taking even small doses of Methotrexate Injection USP daily for less than a week can result in serious side effects, including death.
- Select a day of the week when you are most likely to remember to take Methotrexate Injection USP, and take it on that same day each week.
- Each time you refill your prescription, check to see whether the dose you need to take has changed.

Methotrexate Injection USP is often given together with certain other medicines. If you are using a combination of medicines, make sure that you take each one at the proper time and do not mix them. Ask your healthcare professional to help you plan a way to remember to take your medicines at the right times.

While you are using Methotrexate Injection USP, your healthcare professional may want you to drink extra fluids so that you will pass more urine. This will help the medicine to pass from your body, and will prevent kidney problems.

Usual dose:

The dose of Methotrexate Injection USP will be different for different patients. Your healthcare professional will tell you how much to take. Your dose will depend on:

- what the medicine is being used for
- your weight
- if you are taking other medicines

Your healthcare professional may start you on a lower dose, may change your dose, stop your treatment for a period of time or recommend that you stop treatment completely. This may happen if:

- you have kidney problems
- you are elderly
- you experience certain side effects
- your condition gets worse

Overdose:

If you take too much Methotrexate Injection USP you might get mouth ulcers, feel tired or weak, or experience bleeding, nausea, vomiting, diarrhea, skin rash or fever.

If you think you, or a person you are caring for, have taken too much Methotrexate Injection USP, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

Missed Dose:

If you missed a scheduled dose, contact your healthcare professional for instructions.

What are possible side effects from using Methotrexate Injection USP?

These are not all the possible side effects you may have when taking Methotrexate Injection USP. If you experience any side effects not listed here, tell your healthcare professional.

Methotrexate Injection USP might cause other unwanted effects that may not occur until months or years after the medicine is used. These delayed effects may include certain types of cancer, such as leukemia. Discuss these possible side effects with your healthcare professional.

Side effects may include:

- nausea, stomach pain
- loss of appetite
- weight loss
- hoarseness
- dizziness
- headaches
- hair loss
- mood changes
- confusion
- ringing in the ears
- sore eyes, blurred vision
- skin rashes, pin-point red spots on the skin, reddening or whitening of the skin, acne, boils
- fatigue, drowsiness, weakness
- chills and fever
- impotence, loss of interest in sex
- painful muscles and joints
- swelling in areas of the body that do not involve the injection sites, including vagina

Methotrexate Injection USP commonly causes nausea and vomiting. Even if you begin to feel ill, do not stop using this medicine without first checking with your healthcare professional. Talk to your healthcare professional for ways to manage these side effects.

Serious side effects, and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
COMMON			
Gastrointestinal problems: diarrhea, vomiting, dehydration, abdominal pain, mouth ulcers			√
Infections: sore throat, fever, chills, swelling of lymph nodes/glands		√	
Lung problems including lung damage and Pneumonitis and Pneumonia (inflammation of the lungs): persistent dry, non-productive cough, shortness of breath, fever, chest pain, sweating, shaking chills		√	
LESS COMMON			

Serious side effects, and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Pericarditis, Pericardial effusion (inflammation of the lining of the heart or build up of fluid around the heart): chest pain or pressure, sharp, stabbing chest pain that gets worse when you cough, swallow, breathe deeply or lie flat, shortness of breath			√
Blood problems (low white or red blood cells or platelets): shortness of breath, weakness, frequent infections, cold sores, pale skin, rapid heart rate, fatigue, fever, heavy bleeding or bleeding for longer than usual if you hurt yourself, bruising easily			√
RARE			
Allergic reaction: skin rash, itching, chest tightness, wheezing, dizziness, hives, faintness, rapid heartbeat, shortness of breath, and/or a swollen face, lips or tongue			√
Gastrointestinal problems: blood in stool, bloody vomit, black tarry stools			√
Kidney problems: pain or difficulty urinating, lower back or side pain, blood in urine, changes in how often or how much you urinate, swelling of the hands, ankles or feet, nausea, vomiting		√	
Liver problems (including hepatitis): yellowing of your eyes or skin, itching, right upper stomach pain or swelling, nausea or vomiting, dark urine, pale stool			√
UNKNOWN			
Nervous system problems including Leukoencephalopathy /Encephalitis / Encephalopathy (brain disorders): abnormal			√

Serious side effects, and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
reflexes, paralysis, abnormal behaviours, loss of consciousness, headache, weakness or unable to move a muscle or group of muscles on one or both sides of the body, stroke-like episodes, difficulty speaking, coma, disorientation, changes or reduced senses of touch or temperature, numbness or feelings of prickling (pins and needles), short term blindness, seizures, vomiting, loss of speech and sight, changes in thinking, memory and orientation, personality changes			
Drug reaction with eosinophilia and systemic symptoms (DRESS) (serious skin reaction that may affect one or more organ): fever, severe rash, peeling skin, swollen lymph nodes/glands, flu-like feeling, yellow skin or eyes, shortness of breath, dry cough, chest pain or discomfort, feeling thirsty, urinating less often less urine			√
Pulmonary alveolar hemorrhage (bleeding in the lungs): suddenly spit or cough up blood			√
Reactions at the injection site: blistering, itching, pain, redness, severe skin damage, tenderness, warmth in the area around the injection	√		
Sepsis and septic shock (blood infections): fever or dizziness, chills, high or very low body temperature, little or no urine, low blood pressure, rapid breathing and heart beat		√	
Convulsions: seizure, shaking or fits			√

Serious side effects, and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Diabetes (condition where the body does not produce enough insulin): excessive eating, thirst, and urination; unexplained weight loss, poor wound healing, infections		√	
Osteonecrosis of the jaw (tiny breaks in a bone leading to eventual collapse): broken bones, jaw pain		√	
Osteoporosis (thinning of the bones): broken bones, pain, back pain that gets worse when standing or walking		√	
Lymphoma (lymphatic system cancer): painless swelling of lymph nodes/glands, swollen tonsils, night sweats, itching, unexplained weight loss, persistent coughing/difficulty breathing or not being able to breathe		√	
Toxic Epidermal Necrolysis (TEN), Stevens Johnson syndrome (SJS), Erythema multiforme (severe skin reactions): redness, blistering and/or peeling of large areas of the skin, raised red or purple skin patches, possibly with blister or crust in the center; possibly swollen lips, mild itching or burning			√
Chemical arachnoiditis (rare pain disorder due to inflammation of a membrane surrounding the nerves of the spinal cord): headache, back pain, neck stiffness, fever		√	
Hypotension (low blood pressure): dizziness, fainting, light-headedness, blurred vision, nausea, vomiting, fatigue		√	
Lymphoproliferative disorders (excessive growth of white blood cells): enlarged lymph		√	

Serious side effects, and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
nodes/glands, abnormal bleeding, joint pain, bruising, diarrhea, nausea, vomiting, headache			
Reactivation of chronic infections like herpes zoster, tuberculosis, hepatitis B, hepatitis C (when a previous infection becomes active again): rash that is painful, itchy or tingling, cough, fever, weight loss, joint pain and inflammation, fatigue, loss of appetite, nausea, yellowing of the skin or whites of eyes, abdominal pain		√	
Thrombosis (blood clots): chest pain, shortness of breath, dizziness, face drooping, slurred speech, swelling, pain, arm or leg may be warm to the touch and appear red			√
Tumour lysis syndrome (the sudden, rapid death of cancer cells due to the treatment): nausea, shortness of breath, irregular heartbeat, heart rhythm disturbances, lack of urination, clouding of urine, muscle spasms or twitching, tiredness and/or joint pain, severe muscle weakness, and seizures. Metabolic disorders (kidney failure, abnormal heartbeat) and abnormal blood tests due to rapid breakdown of cancer cells			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store Methotrexate Injection USP without preservative between 15°C and 25°C and away from direct light. Avoid freezing. Discard any unused solution.

Store Methotrexate Injection USP with preservative (benzyl alcohol) between 15°C and 25°C. Once the vials have been punctured they can be stored between 2°C and 8°C for a maximum of four weeks (30 days). Protect from light and freezing. Aseptic techniques should be used when handling punctured vials to avoid contamination.

Keep vials of Methotrexate Injection USP in the carton until time of use. The Methotrexate Injection USP vial should be inspected for damage and visible signs of leaks. If there are signs of breakage or leakage from the vial, do not use.

Do not keep expired medicine or medicine that you no longer need. Be sure that any discarded medicine is out of the reach of children.

Keep out of reach and sight of children.

If you want more information about Methotrexate Injection USP

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website <https://www.pfizer.ca>, or by calling 1-800-463-6001

This leaflet was prepared by Pfizer Canada ULC, Kirkland, Québec H9J 2M5

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