

Methotrexate

About This Drug

Methotrexate is used to treat cancer. This drug is given in the vein (IV), as an injection under the skin (subcutaneously), in your muscle (intramuscularly), orally (by mouth), or as an injection into the fluid that surrounds the brain and spinal cord (intrathecally).

Possible Side Effects

- Decrease in the number of white blood cells. This may raise your risk of infection.
- Soreness of the mouth and throat. You may have red areas, white patches, or sores that hurt.
- Nausea
- Pain in your abdomen

Note: All possible side effects are not included. Your side effects may be different depending on your cancer diagnosis, condition, or if you are receiving other drugs in combination. Please discuss any concerns or questions with your medical team.

Warnings and Precautions

- Severe bone marrow suppression, which is a decrease in the number of white blood cells, red blood cells, and platelets, which can be life-threatening. This may raise your risk of infection, make you tired and weak, and raise your risk of bleeding.
- Changes in your kidney function which can cause kidney failure
- Changes in your liver function, which cause liver failure and be life-threatening
- Severe nausea, vomiting, diarrhea, inflammation (swelling) of your intestines or stomach may occur, or an abnormal hole may develop in intestine, which can be life-threatening. Sores in your mouth may become severe.
- This drug may raise your risk of getting a second cancer, such as lymphoma.
- Inflammation (swelling) of the lungs which can be life-threatening. You may have a dry cough or trouble breathing.
- Tumor lysis syndrome: This drug may act on the cancer cells very quickly. This may affect how your kidneys work.
- Risk of severe and life-threatening infections
- Changes in your central nervous system can happen, which can be life-threatening. The central nervous system is made up of your brain and spinal cord. You could feel extreme tiredness, agitation, confusion, hallucinations (see or hear things that are not there), trouble understanding

or speaking, loss of control of your bowels or bladder, eyesight changes, numbness, or lack of strength to your arms, legs, face, or body, seizures, and coma. **If you start to have any of these symptoms call your doctor right away.**

- Severe allergic skin reaction, which can be life-threatening. You may develop blisters on your skin that are filled with fluid or a severe red rash all over your body that may be painful.
- Allergic reactions, including anaphylaxis are rare but may happen in some patients. Signs of allergic reaction to this drug may be swelling of the face, feeling like your tongue or throat are swelling, trouble breathing, rash, itching, fever, chills, feeling dizzy, and/or feeling that your heart is beating in a fast or not normal way. **If this happens, do not take another dose of this drug. You should get urgent medical treatment.**
- If you receive radiation while also taking methotrexate, you are at an increased risk of infection and damage to your tissues, muscles, and bones.
- If you have received radiation treatments, your skin may become red after methotrexate. This reaction is called “radiation recall.” Your body is recalling, or remembering, that it had radiation therapy.

Note: *Some of the side effects above are very rare. If you have concerns and/or questions, please discuss them with your medical team.*

Important Information

- Talk to your doctor before receiving any vaccinations during your treatment. Some vaccinations are not recommended while receiving methotrexate.
- If you are getting this drug by injection into the fluid that surrounds the brain and spinal cord (intrathecal), your side effects might be different than those listed above. Please talk to your doctor about these side effects.
- Side effects may be more severe if you are receiving high doses of this medication. When receiving moderate or high doses of methotrexate, you may also receive a medication called leucovorin, which helps decrease the side effects of methotrexate. Please follow the administration instructions from your medical team very closely.

How to Take Your Medication

- **For oral only:** Take this medicine as prescribed by your doctor and the medicine label. Severe side effects and death have happened in people taking the medicine incorrectly.
- **Missed dose:** If you vomit or miss a dose, contact your doctor for instruction. Do not take 2 doses at the same time or extra doses.
- **Handling:** Wash your hands after handling your medicine, your caretakers should not handle your medicine with bare hands and should wear latex gloves.
- This drug may be present in the saliva, tears, sweat, urine, stool, vomit, semen, and vaginal secretions. Talk to your doctor and/or your nurse about the necessary precautions to take during this time.
- **Storage for oral only:** Store this medicine in the original container at room temperature. Protect from light.
- **Disposal of unused oral medicine:** Do not flush any expired and/or unused medicine down the toilet or drain unless you are specifically instructed to do so on the medication label. Some facilities



have take-back programs and/or other options. If you do not have a take-back program in your area, then please discuss with your nurse or your doctor how to dispose of unused medicine.

Treating Side Effects

- Manage tiredness by pacing your activities for the day.
- Be sure to include periods of rest between energy-draining activities.
- To decrease the risk of infection, wash your hands regularly.
- Avoid close contact with people who have a cold, the flu, or other infections.
- Take your temperature as your doctor or nurse tells you, and whenever you feel like you may have a fever.
- To help decrease the risk of bleeding, use a soft toothbrush. Check with your nurse before using dental floss.
- Be very careful when using knives or tools.
- Use an electric shaver instead of a razor.
- Drink plenty of fluids (a minimum of eight glasses per day is recommended).
- Mouth care is very important. Your mouth care should consist of routine, gentle cleaning of your teeth or dentures and rinsing your mouth with a mixture of 1/2 teaspoon of salt in 8 ounces of water or 1/2 teaspoon of baking soda in 8 ounces of water. This should be done at least after each meal and at bedtime.
- If you have mouth sores, avoid mouthwash that has alcohol. Also avoid alcohol and smoking because they can bother your mouth and throat.
- If you throw up or have diarrhea, you should drink more fluids so that you do not become dehydrated (lack of water in the body from losing too much fluid).
- To help with nausea and vomiting, eat small, frequent meals instead of three large meals a day. Choose foods and drinks that are at room temperature. Ask your nurse or doctor about other helpful tips and medicine that is available to help stop or lessen these symptoms.
- If you have diarrhea, eat low-fiber foods that are high in protein and calories and avoid foods that can irritate your digestive tracts or lead to cramping.
- Ask your nurse or doctor about medicine that can lessen or stop your diarrhea.
- Keeping your pain under control is important to your well-being. Please tell your doctor or nurse if you are experiencing pain.
- Use sunscreen when you are outdoors even for a short time. Cover up when you are out in the sun. Wear wide-brimmed hats, long-sleeved shirts, and pants. Keep your neck, chest, and back covered.
- If you received radiation, and your skin becomes red or irritated again, follow the same care instructions you did during radiation treatment. Be sure to tell the nurse or doctor administering your chemotherapy about your skin changes.
- If you get a rash do not put anything on it unless your doctor or nurse says you may. Keep the area around the rash clean and dry. Ask your doctor for medicine if your rash bothers you.

Food and Drug Interactions

- There are no known interactions of methotrexate with food.
- Check with your doctor or pharmacist about all other prescription medicines and over-the-counter medicines and dietary supplements (vitamins, minerals, herbs, and others) you are taking before



starting this medicine as there are known drug interactions with methotrexate. Also, check with your doctor or pharmacist before starting any new prescription or over-the-counter medicines, or dietary supplements to make sure that there are no interactions.

- Folic acid supplements may interfere with how methotrexate works. Folic acid may be in your multivitamin. Check with your doctor or pharmacist before taking any forms of folic acid.
- Non-steroidal anti-inflammatory drugs (NSAIDs) – (e.g., ibuprofen and naproxen) and salicylates (e.g., aspirin) can interact with methotrexate and cause serious harm or even death. Talk with your doctor or pharmacist before taking any NSAIDs or salicylate medications, or if you are unsure if your medication is an NSAID or salicylate.
- Do not drink alcohol while taking this medicine. Alcohol may increase some of the side effects of methotrexate and may increase the risk of changes in your liver function.
- Nitrous oxide anesthesia, also known as laughing gas, can interact with methotrexate and increase the risk of side effects. Check with your doctor or dentist before receiving nitrous oxide anesthesia.
- Some medicines used to treat heartburn may interact with methotrexate. Check with your doctor or pharmacist before taking any medications to treat heartburn.

When to Call the Doctor

Call your doctor or nurse if you have any of these symptoms and/or any new or unusual symptoms:

- Fever of 100.4° F (38° C) or higher
- Chills
- Feeling dizzy or lightheaded
- Extreme tiredness, agitation, or confusion
- Hallucinations
- Trouble understanding or speaking
- Loss of control of bowels or bladder
- Blurry vision or changes in your eyesight
- Numbness or lack of strength to your arms, legs, face, or body
- Pain in your chest
- Dry cough
- Wheezing and/or trouble breathing
- Easy bleeding or bruising
- Symptoms of a seizure such as confusion, blacking out, passing out, loss of hearing or vision, blurred vision, unusual smells or tastes (such as burning rubber), trouble talking, tremors or shaking in parts or all of the body, repeated body movements, tense muscles that do not relax, and loss of control of urine and bowels. **If you or your family member suspects you are having a seizure, call 911 right away.**
- Pain in your mouth or throat that makes it hard to eat or drink
- Nausea that stops you from eating or drinking and/or is not relieved by prescribed medicines
- Throwing up more than 3 times a day
- Diarrhea, 4 times in one day or diarrhea with lack of strength or a feeling of being dizzy
- Pain in your abdomen that does not go away



- Difficulty swallowing
- Flu-like symptoms: fever, headache, muscle and joint aches, and fatigue (low energy, feeling weak)
- Decreased or very dark urine
- Swelling of the hands, feet, or any other part of the body
- A new rash or a rash that is not relieved by prescribed medicines
- Signs of infection: fever or chills, cough, trouble breathing, severe pain in your abdomen, difficulty urinating, burning or pain when you pass urine, redness and/or swelling of the skin
- Signs of possible liver problems: dark urine, pale bowel movements, pain in your abdomen, feeling very tired and weak, unusual itching, or yellowing of the eyes or skin
- Signs of tumor lysis: confusion or agitation, decreased urine, nausea/vomiting, diarrhea, muscle cramping, numbness and/or tingling, seizures.
- Signs of allergic reaction: swelling of the face, feeling like your tongue or throat are swelling, trouble breathing, rash, itching, fever, chills, feeling dizzy, and/or feeling that your heart is beating in a fast or not normal way. **If you or your family member suspects you are having an allergic reaction, call 911 right away.**
- Pain that does not go away or is not relieved by prescribed medicine
- If you think you are pregnant or may have impregnated your partner

Reproduction Warnings

- **Pregnancy warning:** This drug can have harmful effects on the unborn baby. Women of childbearing potential should use effective methods of birth control during your cancer treatment and for 6 months after stopping treatment. Let your doctor know right away if you think you may be pregnant. Men with female partners of childbearing potential should use effective methods of birth control during your cancer treatment and for 3 months after stopping treatment. Let your doctor know right away if you think you may have impregnated your partner.
- **Breastfeeding warning:** Women should not breastfeed during treatment and for 1 week after stopping treatment because this drug could enter the breast milk and cause harm to a breastfeeding baby.
- **Fertility warning:** In men and women both, this drug may affect your ability to have children in the future. Talk with your doctor or nurse if you plan to have children. Ask for information on sperm or egg banking.

Revised February 2023

