

Methotrexate: What to Expect

When your loved one has been affected by osteosarcoma, chemotherapy may be part of the treatment plan prescribed by your healthcare provider. This brochure can help you understand what to expect during treatment with the chemotherapy medicine, methotrexate.

What is methotrexate?

Methotrexate (meth-o-TREX-ate) is a chemotherapy medicine used to treat many types of cancers in adults and children. Certain types of cancers, like osteosarcoma, are treated with high doses of methotrexate. High-dose methotrexate is usually administered in the hospital during an inpatient stay and is given with other medicines to help the patient better tolerate the treatment.



Visit **MIBAgents.org** for valuable resources to support caregivers and patients with osteosarcoma.



"When it comes to high-dose methotrexate, I would tell other osteosarcoma families to know the side effects, ask questions, and do research."

– Caregiver for a child with osteosarcoma

How does methotrexate work to treat cancer?

All cells in the body need to make their own DNA to reproduce and repair themselves. Methotrexate prevents cells from making DNA, which stops them from making more cells and eventually causes them to die.

How does methotrexate know which cells in the body are cancer cells?

Cancer cells reproduce more quickly than most healthy cells, so methotrexate will have a greater impact on their ability to make more cells. However, as with most chemotherapy treatments, methotrexate can affect both cancer cells and healthy cells. Shortly after receiving methotrexate, additional medicine is also given that helps protect those healthy cells from damage.

How long does methotrexate stay in the body?

After methotrexate carries out its therapeutic effects in the body, it is removed by the kidneys and leaves the body in the urine. Full clearance of methotrexate from the body can take several days. Many factors can affect how well one person's body clears methotrexate, and every person is different. It is important to know that there may be cases where clearance takes longer than expected, and the time it takes to clear methotrexate may be different from one cycle of therapy to the next. During the time it takes for methotrexate to leave the body, the patient will usually have to remain in the hospital and have blood drawn regularly to monitor their rate of clearance.



"Before my first treatment, I wish I would have known that the amount of time it will take to clear methotrexate completely varies."

– Patient with osteosarcoma

What does it mean to have delayed methotrexate clearance?

Sometimes, the body may not clear methotrexate as quickly as it should. When the levels of methotrexate in the body remain high for too long, this is known as *delayed methotrexate clearance* and can increase the risk of damage to healthy cells and organs. Delayed methotrexate clearance is a serious problem because it can lead to lasting injury to the kidneys, mouth, gut, and immune system and can interrupt future courses of cancer treatment.

How common is delayed methotrexate clearance?

Any patient receiving methotrexate, regardless of known risk factors, may experience delayed clearance. It's estimated that up to 12% of patients who receive high-dose methotrexate may experience delayed clearance if their kidneys are not working well enough.



Some medicines and vitamins may impact the body's ability to clear methotrexate.

These include:

- Over-the-counter pain medicines
 - Ibuprofen, naproxen, aspirin or other salicylates
- Some prescription antibiotics
 - Penicillin and penicillin derivatives, probenecid, trimethoprim sulfamethoxazole, vancomycin, aminoglycosides
- Over-the-counter heartburn medicines, also known as proton pump inhibitors (PPIs)
- Other medicines and vitamins
 - Cyclosporine, amphotericin B, radiographic contrast, prior platinum-based chemotherapy, vitamin C

This is not a complete list of all the medicines that affect methotrexate clearance or interact with methotrexate. Always inform your doctor and pharmacist of any prescription or over-the-counter medicines, vitamins, or herbal supplements being taken.



Are some patients more likely than others to experience delayed methotrexate clearance?

Taking certain medications or having risk factors such as poor kidney function, prior side effects with methotrexate, fluid loss, or poor fluid intake can increase the chance of experiencing delayed clearance. Having certain acidic foods and beverages before or during treatment may also affect methotrexate clearance.

Is there anything that can be done to help prevent delayed methotrexate clearance?

When high-dose methotrexate is given, the kidneys have to work harder than normal to clear methotrexate from the body, so it's especially important to keep the kidneys functioning well during this time. Although there isn't a guaranteed way to prevent delayed methotrexate clearance, there are a few things you and your doctors can do to help reduce the risk. Sodium bicarbonate is a treatment that helps counteract acid and is usually given through an IV along with large amounts of fluids to help protect the kidneys during and after treatment with methotrexate. Staying hydrated and avoiding foods and drinks with licorice or high acid content (like soda and some fruit juices) can also help keep the kidneys working well to process and clear methotrexate.

Are there signs or symptoms of delayed methotrexate clearance I should watch for?

It's important for delayed methotrexate clearance to be treated promptly. Your healthcare team is there for you and will be watching closely for any signs of delayed clearance. There are also signs you can watch for that may help them detect delayed clearance early.

Alert your healthcare provider if you observe:



Decrease in urine output



Sudden changes in weight



Your healthcare team will also be watching for any signs that methotrexate may be having an effect on healthy cells in the body.

Tell your healthcare provider right away if you notice any of the following signs:

- Rash
- Fever, chills, dry cough, trouble breathing
- Headaches, back pain, stiff neck
- Confusion, weakness, seizures, temporary blindness, paralysis, mood changes, sleepiness, problems with coordination
- Mouth sores, vomiting, diarrhea

These are not all the possible side effects of high-dose methotrexate treatment. You know your loved one best, so contact your healthcare provider if you have any questions or if you notice any symptoms or changes that concern you.

Prompt treatment of delayed methotrexate clearance will allow you and your healthcare team to:



Avoid damage to healthy organs and tissues



Ensure cancer treatment continues as planned

Beginning cancer therapy can feel overwhelming, but knowing what to expect can help. During treatment with high-dose methotrexate, be prepared for the time it might take the body to clear this medicine. Clearance can take several days, and every person is different.

Remember: Your healthcare team will be watching for any signs or symptoms of delayed clearance so the appropriate care can be given quickly to help keep the cancer treatment plan on track.

Talk to your healthcare provider if you have any further questions about what to expect during treatment with methotrexate.



Visit **MIBAgents.org** to learn more about osteosarcoma and access free resources for caregivers and patients with osteosarcoma.



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