

Cyclophosphamide IV Formulation (Cytoxan®, Neosar®, Endoxan®)

Pronounce: SYE-kloe-FOS-fa-mide

Classification: Alkylating Agent

About Cyclophosphamide IV Formulation (Cytoxan®, Neosar®, Endoxan®)

Cyclophosphamide kills cancer cells through a process called alkylation. Alkylation damages the DNA of cells, which prevents them from dividing and causes them to die. Since cancer cells tend to divide faster and with less error correcting than healthy cells, cancer cells are more sensitive to this damage.

How to Take Cyclophosphamide

Cyclophosphamide can be given by intravenous (IV, into a vein) infusion or taken orally (by mouth) in a pill form. This information is about the IV formulation. Your dose and schedule are determined by your size and type of cancer being treated.

This medication can interact with a number of medications including: metronidazole, tamoxifen, warfarin, cyclosporine amiodarone, Echinacea, and thiazide diuretics, among others. Be sure to tell your healthcare provider about all medications and supplements you take.

Possible Side Effects

There are a number of things you can do to manage the side effects of cyclophosphamide. Talk to your care team about these recommendations. They can help you decide what will work best for you. There are some of the most common or important side effects:

Infection and Low White Blood Cell Count (Leukopenia or Neutropenia)

This medication can cause life threatening infections, with or without a decrease in white blood cell counts.

White blood cells (WBC) are important for fighting infection. While receiving treatment, your [WBC count can drop](#), putting you at a higher risk of getting an infection. You should let your doctor or nurse know right away if you have a fever (temperature greater than 100.4°F or 38°C), sore throat or cold, shortness of breath, cough, burning with urination, or a sore that doesn't heal.

Tips to preventing infection:

- [Washing hands](#), both yours and your visitors, is the best way to prevent the spread of infection.
- Avoid large crowds and people who are sick (i.e.: those who have a cold, fever or cough or live with someone with these symptoms).
- When working in your yard, wear protective clothing including long pants and gloves.
- Do not handle pet waste.
- Keep all cuts or scratches clean.
- Shower or bathe daily and perform frequent [mouth care](#).

- Do not cut cuticles or ingrown nails. You may wear nail polish, but not fake nails.
- Ask your oncology care team before scheduling dental appointments or procedures.
- Ask your oncology care team before you, or someone you live with, has any vaccinations.

Low Red Blood Cell Count (Anemia)

Your red blood cells are responsible for carrying oxygen to the tissues in your body. When the [red cell count is low](#), you may feel tired or weak. You should let your oncology care team know if you experience any shortness of breath, difficulty breathing or pain in your chest. If the count gets too low, you may receive a blood transfusion.

Low Platelet Count (Thrombocytopenia)

Platelets help your blood clot, so when the [count is low](#) you are at a higher risk of bleeding. Let your oncology care team know if you have any excess bruising or bleeding, including nose bleeds, bleeding gums or blood in your urine or stool. If the platelet count becomes too low, you may receive a transfusion of platelets.

- Do not use a razor (an electric razor is fine).
- Avoid contact sports and activities that can result in injury or bleeding.
- Do not take aspirin (salicylic acid), non-steroidal, anti-inflammatory medications (NSAIDs) such as Motrin/Advil (ibuprofen), Aleve (naproxen), Celebrex (celecoxib) etc. as these can all increase the risk of bleeding. Please consult with your healthcare team regarding use of these agents and all over the counter medications/supplements while on therapy.
- Do not floss or use toothpicks and use a soft-bristle toothbrush to brush your teeth.

Nausea and/or Vomiting

Talk to your oncology care team so they can prescribe medications to help you manage [nausea and vomiting](#). In addition, dietary changes may help. Avoid things that may worsen the symptoms, such as heavy or greasy/fatty, spicy or acidic foods (lemons, tomatoes, oranges). Try saltines, or ginger ale to lessen symptoms.

Call your oncology care team if you are unable to keep fluids down for more than 12 hours or if you feel lightheaded or dizzy at any time.

Diarrhea

Your oncology care team can recommend medications to relieve [diarrhea](#). Also, try eating [low-fiber](#), bland foods, such as white rice and boiled or baked chicken. Avoid raw fruits, vegetables, whole grain breads, cereals and seeds. Soluble fiber is found in some foods and absorbs fluid, which can help relieve diarrhea. Foods high in soluble fiber include: applesauce, bananas (ripe), canned fruit, orange sections, boiled potatoes, white rice, products made with white flour, oatmeal, cream of rice, cream of wheat, and farina. Drink 8-10 glasses of non-alcoholic, un-caffeinated fluid a day to prevent dehydration.

Loss or Thinning of Scalp and Body Hair (Alopecia)

Your hair may become [thin, brittle, or may fall out](#). This typically begins two to three weeks after treatment starts. This hair loss can be all body hair, including pubic, underarm, legs/arms, eyelashes, and nose hairs. The use of scarves, wigs, hats and hairpieces may help. Hair generally starts to regrow soon after treatment is completed. Remember your hair helps keep you warm in cold weather, so a hat is particularly important in cold weather or to protect you from the sun.

Nail and Skin Changes

Your fingernails/toenails may become dark, brittle or fall off. You may notice dry skin or changes in the color or tone of your skin. Your skin may be more sensitive to the sun, which can result in severe sunburn or rash. Sun sensitivity can last even after chemotherapy is completed. Avoid the sun between 10-2pm, when it is strongest. Wear sunscreen (at least SPF 15) everyday, wear sunglasses and long sleeves/pants to protect your

skin. Keep your fingernails and toenails clean and dry. You may use nail polish, but do not wear fake nails. If any nails fall off, clean the nail bed well with soap and water and cover with a band aid.

Important but Less Common Side Effects

- **Bladder Irritation:** Cyclophosphamide may irritate your bladder and can cause blood in your urine or pain with urination. Drink at least 6 to 8 glasses of fluid per day to flush out your bladder. You may be given IV fluids along with this medication to help lower the chance of bladder irritation. Let your care team know if you have a hard time urinating, have pain or pink/red urine, or bleed with urination. When given in high doses, your provider may give you a medication to protect your bladder.
- **Secondary Malignancies:** There is a very low risk of developing leukemia or another type of cancer due to treatment with this medication, which can happen many years after treatment. This is most often linked to repeated treatments or high doses.
- **Electrolyte Abnormalities:** This medication can affect the normal levels of electrolytes (sodium, potassium, magnesium, calcium, etc.) in your body. Your levels will be monitored using blood tests. If your levels become too low, your care team may prescribe specific electrolytes to be given by IV or taken by mouth. Do not take any supplements without first consulting with your care team.
- **Lung Changes:** This medication may cause lung changes, including pneumonitis (irritation of the lung tissue) and pulmonary fibrosis (a scarring and stiffening of the lung tissue). These problems can develop during treatment, or months to years after treatment is completed. Call your provider right away if you have new or worsening shortness of breath, cough, wheezing or difficulty breathing.
- **Heart Problems:** This medication can affect your heart function and can cause abnormal heartbeats or an abnormal heart rhythm called QT prolongation. Call your provider right away if you develop swelling of the feet or ankles, shortness of breath, have rapid weight gain, feel abnormal heartbeats, or if you feel dizzy or faint.
- **Wound Healing:** This medication can lead to slower or incomplete wound healing, such as a surgical wound not healing or staying closed. Be sure to inform the team performing the surgical procedure that you are taking this drug. You should also inform your oncology team that a surgical procedure is planned. It is recommended that this medication be discontinued prior to any surgery. In addition, any surgical incision should be fully healed prior to starting or restarting the medication. If you have a surgical wound that has not healed or begins to have signs of infection (redness, swelling, warmth), report this to your healthcare team.
- **Veno-occlusive Liver Disease:** This medication can cause blood clots in the small veins of your liver. This can lead to liver failure. If you feel like there is fluid in your belly or notice that your skin or the whites of your eyes are yellowing, contact your care team right away.

Reproductive Concerns

This medication may affect your reproductive system, resulting in the menstrual cycle or sperm production becoming irregular or stopping permanently. Women may experience menopausal effects including hot flashes and [vaginal dryness](#). In addition, the desire for sex may decrease during treatment. You may want to consider sperm banking or egg harvesting if you may wish to have a child in the future. Discuss these options with your oncology team.

Exposure of an unborn child to this medication could cause birth defects, so you should not become pregnant or father a child while on this medication. For women, effective birth control is necessary during treatment and for at least 1 year after treatment. For men, effective birth control is necessary during treatment and for at least 4 months after treatment. Even if your menstrual cycle stops or you believe you are not producing sperm, you could still be fertile and conceive. You should not breastfeed during treatment and for at least 1 week after your last dose.

Fluorouracil (Adrucil®, 5-FU)

Pronounce: flure-oh-YOOR-a-sil

Classification: Antimetabolite

About Fluorouracil (Adrucil®, 5-FU)

An antimetabolite medication affects how DNA is made in cells. Cancer cells divide faster and with less error correction than healthy cells, making them more sensitive to these effects.

Fluorouracil changes how cancer cells make and use DNA and RNA. Fluorouracil prevents cancer cells from making important proteins, which causes cell death and can slow or stop cancer from growing.

How to Take Fluorouracil

Fluorouracil is given as an intravenous (IV, into a vein) infusion. How long the infusion takes depends on your treatment regimen. The dose will be determined by your care team. It can be given alone or with other medications.

If you take warfarin, your INR and PT levels will be closely monitored to adjust your warfarin dose as needed. Please make sure your healthcare team is aware of all the medicines you take before you begin treatment.

Possible Side Effects of Fluorouracil

There are a number of things you can do to manage the side effects of fluorouracil. Talk to your care team about these recommendations. They can help you decide what will work best for you. These are some of the most common or important side effects:

Low White Blood Cell Count (Leukopenia or Neutropenia)

White blood cells (WBC) are important for fighting infection. While receiving treatment, your [WBC count can drop](#), putting you at a higher risk of getting an infection. You should let your doctor or nurse know right away if you have a fever (temperature greater than 100.4°F or 38°C), sore throat or cold, shortness of breath, cough, burning with urination, or a sore that doesn't heal.

Tips to preventing infection:

- [Washing hands](#), both yours and your visitors, is the best way to prevent the spread of infection.
- Avoid large crowds and people who are sick (i.e.: those who have a cold, fever or cough or live with someone with these symptoms).
- When working in your yard, wear protective clothing including long pants and gloves.
- Do not handle pet waste.
- Keep all cuts or scratches clean.
- Shower or bathe daily and perform frequent [mouth care](#).
- Do not cut cuticles or ingrown nails. You may wear nail polish, but not fake nails.
- Ask your oncology care team before scheduling dental appointments or procedures.
- Ask your oncology care team before you, or someone you live with has any vaccinations.

Low Red Blood Cell Count (Anemia)

Your red blood cells are responsible for carrying oxygen to the tissues in your body. When the [red cell count is low](#), you may feel tired or weak. You should let your oncology care team know if you experience any shortness of breath, difficulty breathing, or pain in your chest. If the count gets too low, you may receive a blood

transfusion.

Low Platelet Count (Thrombocytopenia)

Platelets help your blood clot, so when the [count is low](#) you are at a higher risk of bleeding. Let your oncology care team know if you have any excess bruising or bleeding, including nose bleeds, bleeding gums, or blood in your urine or stool. If the platelet count becomes too low, you may receive a transfusion of platelets.

- Do not use a razor (an electric razor is fine).
- Avoid contact sports and activities that can result in injury or bleeding.
- Do not take aspirin (salicylic acid), non-steroidal, anti-inflammatory medications (NSAIDs) such as Motrin/Advil (ibuprofen), Aleve (naproxen), Celebrex (celecoxib), etc. as these can all increase the risk of bleeding. Please consult with your healthcare team regarding the use of these agents and all over-the-counter medications/supplements while on therapy.
- Do not floss or use toothpicks and use a soft-bristle toothbrush to brush your teeth.

Diarrhea

Your oncology care team can recommend medications to relieve [diarrhea](#). Also, try eating [low-fiber](#), bland foods, such as white rice and boiled or baked chicken. Avoid raw fruits, vegetables, whole grain breads, cereals, and seeds. Soluble fiber is found in some foods and absorbs fluid, which can help relieve diarrhea. Foods high in soluble fiber include applesauce, bananas (ripe), canned fruit, orange sections, boiled potatoes, white rice, products made with white flour, oatmeal, cream of rice, cream of wheat, and farina. Drink 8-10 glasses of non-alcoholic, uncaffeinated fluid a day to prevent dehydration.

Mouth Ulcers (Mucositis)

Certain cancer treatments can cause [sores or soreness in your mouth](#) and/or throat. Notify your oncology care team if your mouth, tongue, inside of your cheek, or throat becomes white, ulcerated, or painful. Performing [regular mouth care](#) can help prevent or manage mouth sores. If mouth sores become painful, your doctor or nurse can recommend a pain reliever.

- Brush with a soft-bristle toothbrush or cotton swab twice a day.
- Avoid mouthwashes that contain alcohol. A baking soda and/or salt with warm water mouth rinse (2 level teaspoons of baking soda or 1 level teaspoon of salt in an eight-ounce glass of warm water) is recommended 4 times daily.
- If your mouth becomes dry, eat moist foods, drink plenty of fluids (6-8 glasses), and suck on sugarless hard candy.
- Avoid smoking and chewing tobacco, drinking alcoholic beverages and citrus juices.

Loss or Thinning of Scalp and Body Hair (Alopecia)

Your hair may become [thin, brittle, or may fall out](#). This typically begins two to three weeks after treatment starts. This hair loss can be all body hair, including pubic, underarm, legs/arms, eyelashes, and nose hairs. The use of scarves, wigs, hats, and hairpieces may help. Hair generally starts to regrow soon after treatment is completed. Remember your hair helps keep you warm in cold weather, so a hat is particularly important in cold weather or to protect you from the sun.

Nail and Skin Changes

Your [fingernails/toenails](#) may become dark, brittle, or fall off. Keep your fingernails and toenails clean and dry. You may use nail polish but do not wear fake nails (gels, acrylics, overlay). If any nails fall off, clean the nail bed well with soap and water and cover with a band-aid.

You may notice dry skin or changes in the color or tone of your skin. Your skin may be more sensitive to the sun, which can result in severe sunburn or rash. Sun sensitivity can last even after chemotherapy is

completed. Avoid the sun between 10-2pm, when it is strongest. Wear sunscreen (at least SPF 30 with UVA/UVB protection) every day and reapply when in the sun for extended periods of time); wear sunglasses with UVA/UVB protection, a hat, and long sleeves/pants to protect your skin and seek out shade whenever possible.

Hand Foot Syndrome

Hand-foot syndrome (HFS) is a skin reaction that appears on the palms of the hands and/or the soles of the feet, as a result of certain chemotherapy agents being absorbed by the skin cells. HFS can begin as a mild tingling, numbness, pins-and-needles feeling, redness or pain, or swelling of the hands and/or feet. This can then progress to painful swelling, blistering, or peeling skin that can interfere with your ability to do normal activities. Be sure to let your oncology team know right away if you notice these symptoms, as they may need to adjust the chemotherapy dose or take a break to allow the skin to heal. Some tips to help prevent HFS include:

- Keep hands and feet clean and dry.
- Avoid tight shoes or socks.
- Avoid activities that put pressure on the palms or soles for 1 week after treatment.
- Apply an alcohol-free moisturizer liberally and often (Avoid moisturizers with perfumes or scents).
- Avoid very hot water for baths and showers.

Nausea and/or Vomiting

Talk to your oncology care team so they can prescribe medications to help you manage **nausea and vomiting**. In addition, dietary changes may help. Avoid things that may worsen the symptoms, such as heavy or greasy/fatty, spicy or acidic foods (lemons, tomatoes, oranges). Try saltines, or ginger ale to lessen symptoms.

Call your oncology care team if you are unable to keep fluids down for more than 12 hours or if you feel lightheaded or dizzy at any time.

Important but Less Common Side Effects

- **Heart Problems:** In some cases, this medication can cause or worsen pre-existing heart problems including congestive heart failure, decreased heart function, and heart attack. Notify your healthcare provider if you have sudden weight gain or swelling in the ankles or legs. If you develop chest pain or pressure, pain in the left arm, back, or jaw, sweating, shortness of breath, clammy skin, nausea, dizziness, or lightheadedness, call 911 or go to the nearest emergency room.
- **Neurotoxicity:** This medication can cause neurological issues such as confusion, disorientation, ataxia (trouble walking), and visual disturbances. Call your provider immediately if you are having any symptoms of a neurological issue.
- **Elevated Ammonia Level:** This medication can cause the level of ammonia in your blood to become too high, which can then affect how your brain is functioning. You will have your labs checked to monitor your ammonia level. Symptoms include ataxia (trouble walking), intellectual impairment, and changes in behavior. Call your provider immediately if you notice any of these symptoms.
- **DPD Gene Mutation:** There is a very rare genetic mutation in the DPD gene that can cause very serious side effects to this medication. Report any worsening or unusual symptoms to your healthcare team immediately.

Sexual & Reproductive Concerns

This medication may affect your reproductive system, resulting in the menstrual cycle or sperm production becoming irregular or stopping permanently. Women may experience menopausal effects including hot flashes and **vaginal dryness**. In addition, the desire for sex may decrease during treatment. You may want to consider sperm banking or egg harvesting if you may wish to have a child in the future. Discuss these options with your

oncology team.

Exposure of an unborn child to this medication could cause birth defects, so you should not become pregnant or father a child while on this medication. Effective birth control is necessary during treatment and for at least 3 months after treatment, even if your menstrual cycle stops or you believe you are not producing sperm. You should not breastfeed while receiving this medication.

Methotrexate (Mexate®, Folex®, Rheumatrex®, Amethopterin, MTX)

Pronounce: meth-oh-TREKS-ate

Classification: Antimetabolite

About Methotrexate (Mexate®, Folex®, Rheumatrex®, Amethopterin, MTX)

Methotrexate interferes with DNA production. This stops cell growth and division, resulting in the slowing or stopping of cancer growth. Since cancer cells, in general, divide faster and with less error-correcting than healthy cells, cancer cells are more sensitive to this damage. Methotrexate competes with folic acid uptake in cells. This results in a folic acid deficiency in these cells and leads to cell death. By affecting the folic acid uptake, methotrexate also alters DNA replication and cell division. Cancer cells take up methotrexate faster than normal cells (because they are rapidly dividing and thus replicate their DNA more frequently), causing their cell death.

Leucovorin is given starting 24 hours after methotrexate. Leucovorin is also known as folinic acid and is converted into a derivative of folic acid in the body. Therefore, Leucovorin is given in an attempt to prevent healthy cells from taking up too much methotrexate, but on the other hand, allowing time for the methotrexate to get into cancer cells to cause their death.

How to Take Methotrexate

Methotrexate is given by intravenous (IV) infusion. In special situations, it may be injected into the spinal cord space (called intrathecal administration). It can also be given by mouth in the form of a tablet. The dosage is based on your body weight, medical condition, and the regimen your physician is using.

***If you have been prescribed leucovorin in combination with methotrexate and are unable to take it, keep it down, or miss a dose, call your healthcare team immediately.**

The blood levels of this medication can be affected by certain foods and medications, so they should be avoided. These include non-steroidal anti-inflammatory (NSAID) medications including ibuprofen, tetracycline, penicillin, sulfamethoxazole/trimethoprim, some other oral antibiotics, and folic acid. Be sure to tell your healthcare provider about all medications and supplements you take.

You, or anyone you live with, should avoid having live or live-attenuated vaccines while receiving this medication. These include herpes zoster (Zostavax) for shingles prevention, oral polio, measles, nasal flu vaccine (FluMist®), rotavirus, and yellow fever vaccines.

Possible Side Effects of Methotrexate

There are a number of things you can do to manage the side effects of Methotrexate. Talk to your care team about these recommendations. They can help you decide what will work best for you. These are some of the most common or important side effects:

Infection and Low White Blood Cell Count (Leukopenia or Neutropenia)

This medication can cause life-threatening infections, with or without a decrease in white blood cell counts.

White blood cells (WBC) are important for fighting infection. While receiving treatment, your [WBC count can drop](#), putting you at a higher risk of getting an infection. You should let your doctor or nurse know right away if you have a fever (temperature greater than 100.4°F or 38°C), sore throat or cold, shortness of breath, cough, burning with urination, or a sore that doesn't heal.

Tips to preventing infection:

- [Washing hands](#), both yours and your visitors, is the best way to prevent the spread of infection.
- Avoid large crowds and people who are sick (i.e.: those who have a cold, fever, or cough or live with someone with these symptoms).
- When working in your yard, wear protective clothing including long pants and gloves.
- Do not handle pet waste.
- Keep all cuts or scratches clean.
- Shower or bathe daily and perform frequent [mouth care](#).
- Do not cut cuticles or ingrown nails. You may wear nail polish, but not fake nails.
- Ask your oncology care team before scheduling dental appointments or procedures.
- Ask your oncology care team before you, or someone you live with has any vaccinations.

Nausea and/or Vomiting

Talk to your oncology care team so they can prescribe medications to help you manage [nausea and vomiting](#). In addition, dietary changes may help. Avoid things that may worsen the symptoms, such as heavy or greasy/fatty, spicy or acidic foods (lemons, tomatoes, oranges). Try saltines, or ginger ale to lessen symptoms.

Call your oncology care team if you are unable to keep fluids down for more than 12 hours or if you feel lightheaded or dizzy at any time.

Mouth Sores (Mucositis)

Certain cancer treatments can cause [sores or soreness in your mouth](#) and/or throat. Notify your oncology care team if your mouth, tongue, inside of your cheek or throat becomes white, ulcerated, or painful. Performing [regular mouth care](#) can help prevent or manage mouth sores. If mouth sores become painful, your doctor or nurse can recommend a pain reliever.

- Brush with a soft-bristle toothbrush or cotton swab twice a day.
- Avoid mouthwashes that contain alcohol. A baking soda and/or salt with warm water mouth rinse (2 level teaspoons of baking soda or 1 level teaspoon of salt in an eight-ounce glass of warm water) is recommended 4 times daily.
- If your mouth becomes dry, eat moist foods, drink plenty of fluids (6-8 glasses), and suck on sugarless hard candy.
- Avoid smoking and chewing tobacco, drinking alcoholic beverages, and citrus juices.

Diarrhea

Your oncology team can recommend medications to relieve [diarrhea](#). Also, try eating [low-fiber](#), bland foods, such as white rice and boiled or baked chicken. Avoid raw fruits, vegetables, whole-grain breads, cereals, and seeds. Soluble fiber is found in some foods and absorbs fluid, which can help relieve diarrhea. Foods high in soluble fiber include applesauce, bananas (ripe), canned fruit, orange sections, boiled potatoes, white rice, products made with white flour, oatmeal, cream of rice, cream of wheat, and farina. Drink 8-10 glasses of non-alcoholic, uncaffeinated fluid a day to prevent dehydration.

Low Red Blood Cell Count (Anemia)

Your red blood cells are responsible for carrying oxygen to the tissues in your body. When the [red cell count is low](#), you may feel tired or weak. You should let your oncology care team know if you experience any shortness of breath, difficulty breathing, or pain in your chest. If the count gets too low, you may receive a blood transfusion.

Low Platelet Count (Thrombocytopenia)

Platelets help your blood clot, so when the [count is low](#) you are at a higher risk of bleeding. Let your oncology care team know if you have any excess bruising or bleeding, including nose bleeds, bleeding gums, or blood in your urine or stool. If the platelet count becomes too low, you may receive a transfusion of platelets.

- Do not use a razor (an electric razor is fine).
- Avoid contact sports and activities that can result in injury or bleeding.
- Do not take aspirin (salicylic acid), non-steroidal, anti-inflammatory medications (NSAIDs) such as Motrin/Advil (ibuprofen), Aleve (naproxen), Celebrex (celecoxib), etc. as these can all increase the risk of bleeding. Please consult with your healthcare team regarding the use of these agents and all over-the-counter medications/supplements while on therapy.
- Do not floss or use toothpicks and use a soft-bristle toothbrush to brush your teeth.

Fatigue

[Fatigue](#) is very common during cancer treatment and is an overwhelming feeling of exhaustion that is not usually relieved by rest. While on cancer treatment, and for a period after, you may need to adjust your schedule to manage fatigue. Plan times to rest during the day and conserve energy for more important activities. Exercise can help combat fatigue; a simple daily walk with a friend can help. Talk to your healthcare team for helpful tips on dealing with this side effect.

Loss or Thinning of Scalp and Body Hair (Alopecia)

Your hair may become [thin, brittle, or may fall out](#). This typically begins two to three weeks after treatment starts. This hair loss can be all body hair, including pubic, underarm, legs/arms, eyelashes, and nose hairs. The use of scarves, wigs, hats, and hairpieces may help. Hair generally starts to regrow soon after treatment is completed. Remember your hair helps keep you warm in cold weather, so a hat is particularly important in cold weather or to protect you from the sun.

Nail and Skin Changes

Your fingernails/toenails may become dark, brittle, or fall off. Keep your fingernails and toenails clean and dry. You may use nail polish but do not wear fake nails (gels, acrylics, overlay). If any nails fall off, clean the nail bed well with soap and water and cover with a band-aid.

You may notice dry skin or changes in the color or tone of your skin. Your skin may be more sensitive to the sun, which can result in severe sunburn or rash. Sun sensitivity can last even after chemotherapy is completed. Avoid the sun between 10-2 p.m., when it is strongest. Wear sunscreen (at least SPF 30 with UVA/UVB protection) every day and reapply when in the sun for extended periods of time; wear sunglasses with UVA/UVB protection, a hat, and long sleeves/pants to protect your skin and seek out shade whenever possible.

Secondary Malignancies

There is a very low risk of developing leukemia, sarcoma, lung cancer, or other types of cancer due to treatment with this medication, which can occur many years after treatment. This is most often associated with repeated treatments or high doses.

Kidney Problems

This medication can cause kidney problems, including an increased creatinine level, which your oncology care team may monitor for using blood tests. Notify your healthcare provider if you notice decreased urine output,

blood in the urine, swelling in the ankles, or loss of appetite.

Tumor Lysis Syndrome

If there are a large number of tumor cells in your body prior to treatment, you are at risk for tumor lysis syndrome. This happens when the tumor cells die too quickly and their waste overwhelms the body. You may be given a medication (allopurinol) and IV fluids to help prevent this. If you experience nausea, vomiting, diarrhea, or become lethargic (drowsy, sluggish), notify your oncology team right away. TLS can affect your kidney function. Your provider will monitor your kidney function with blood work. Notify your provider if you have little or no urine output.

Radiation Recall

Radiation recall is when the administration of a medication causes a skin reaction that looks like a sunburn (redness, swelling, soreness, peeling skin) in areas where radiation was previously given. Notify your oncology team if you notice this side effect. Treatment can include topical steroid ointments and a delay in your next chemotherapy dose.

Important but Less Common Side Effects

- **Lung Changes:** This medication can cause an opportunistic infection called pneumocystis pneumonia. It can also cause interstitial pneumonitis, particularly when high doses have been received. Interstitial pneumonitis can develop months to years after treatment is completed and may be more common in people with pre-existing lung conditions. Notify your healthcare provider if you develop fever, shortness of breath, non-productive cough, wheezing, or difficulty breathing.
- **Liver Toxicity:** This medication can cause liver toxicity, which your oncology care team may monitor using blood tests called liver function tests. Notify your healthcare provider if you notice yellowing of the skin or eyes, your urine appears dark or brown, or you have pain in your abdomen, as these can be signs of liver toxicity.
- **Eye Problems:** This medication can cause your eyes to become irritated or watery and you may be more sensitive to light. Notify your provider if you develop any eye changes.
- **Neurologic changes:** This medication can affect the nervous system, causing you to feel drowsy, dizzy, or confused. Notify your provider if you are feeling different.

Sexual & Reproductive Concerns

This medication may affect your reproductive system, resulting in the menstrual cycle or sperm production becoming irregular or stopping permanently. Women may experience menopausal effects including hot flashes and [vaginal dryness](#). In addition, the desire for sex may decrease during treatment. You may want to consider sperm banking or egg harvesting if you wish to have a child in the future. Discuss these options with your oncology team.

Exposure of an unborn child to this medication could cause birth defects, so you should not become pregnant or father a child while on this medication. Effective birth control is necessary during treatment and for at least 3 months after treatment for men and during treatment and for at least 6 months for women, even if your menstrual cycle stops or you believe you are not producing sperm. You should not breastfeed while receiving this medication or for 1 week after your last dose.

Intrathecal (Spinal) Administration

When injected into the spinal cord space, methotrexate can cause headache, vomiting, fever, or stiff neck. In rare cases, intrathecal administration can cause neurotoxicity, which presents with paralysis, speech difficulty, seizures, or coma. This can occur up to several days after the treatment and resolves in a few days.

Methotrexate Oral Formulation (Trexall®, Rheumatrex®),

MTX)

Pronounce: meth-oh-TREK-sate

Classification: Antimetabolite

About Methotrexate Oral Formulation (Trexall®, Rheumatrex®, MTX)

Methotrexate interferes with DNA production. This stops cell growth and division, resulting in the slowing or stopping of cancer growth. Since cancer cells, in general, divide faster and with less error-correcting than healthy cells, cancer cells are more sensitive to this damage. Methotrexate competes with folic acid uptake in cells. This results in a folic acid deficiency in these cells and leads to cell death. By affecting the folic acid uptake, methotrexate also alters DNA replication and cell division. Cancer cells take up methotrexate faster than normal cells (because they are rapidly dividing and thus replicate their DNA more frequently), causing their cell death.

Depending on your diagnosis, you may also receive leucovorin starting 24 hours after methotrexate. Leucovorin is also known as folinic acid and is converted into a derivative of folic acid in the body. Therefore, leucovorin is given in an attempt to prevent healthy cells from taking up too much methotrexate, while allowing time for the methotrexate to get into cancer cells to cause their death.

How to Take Oral Methotrexate

Methotrexate comes in a tablet taken by mouth. Your dosing schedule will depend on the disease being treated as well as how your body responds to the medication. It is important to follow your healthcare team's dosage instructions carefully. You should not take larger or smaller amounts than prescribed by your healthcare provider.

It is important to make sure you are taking the correct amount of medication every time. Before every dose, check that what you are taking matches what you have been prescribed.

The blood levels of this medication can be affected by certain foods and medications, so they should be avoided. These include: non-steroidal anti-inflammatory (NSAID) medications including ibuprofen, tetracycline, penicillin, sulfamethoxazole/trimethoprim, and other oral antibiotics and folic acid. Be sure to tell your healthcare provider about all medications and supplements you take.

****If you have been prescribed leucovorin in combination with methotrexate and are unable to take it, keep it down or miss a dose, call your healthcare team immediately.***

You, or anyone you live with, should avoid having live or live-attenuated vaccines while receiving this medication. These include herpes zoster (Zostavax) for shingles prevention, oral polio, measles, nasal flu vaccine (FluMist®), rotavirus, and yellow fever vaccines.

Storage and Handling

Store your medication in the original, labeled container at room temperature and in a dry location (unless otherwise directed by your healthcare provider or pharmacist). This medication should not be stored in a pillbox. Keep containers out of reach of children and pets.

If a caregiver prepares your dose for you, they should consider wearing gloves or pour the pills directly from their container into the cap, a small cup, or directly into your hand. They should avoid touching the pills. They should always wash their hands before and after giving you the medication. Pregnant or nursing women should not prepare the dose for you. Ask your oncology team where to return any unused medication for disposal. Do not flush it down the toilet or throw it in the trash.

Where do I get this medication?

Depending on your prescription insurance coverage, oral methotrexate may be available at a retail pharmacy or through a specialty pharmacy. Your oncology team will work with your prescription drug plan to identify an in-network pharmacy for the distribution of this medication.

Insurance Information

This medication may be covered under your prescription drug plan. Patient assistance may be available to qualifying individuals without prescription drug coverage. Co-pay cards, which reduce the patient's co-pay responsibility for eligible commercially (non-government sponsored) insured patients, are also offered by the manufacturer. Co-pay assistance from private third party foundations may be available. Your care team can help you access these resources if they are available.

This medication is covered under Medicare part B for Medicare recipients. Make sure your pharmacist knows to process this prescription through your Medicare part B and NOT part D.

Possible Side Effects of Methotrexate

There are a number of things you can do to manage the side effects of Methotrexate. Talk to your care team about these recommendations. They can help you decide what will work best for you. These are some of the most common or important side effects:

Allergic Reactions

In some cases, patients can have an allergic reaction to this medication. Signs of a reaction can include: shortness of breath or difficulty breathing, chest pain, rash, flushing or itching, or a decrease in blood pressure. If you notice any changes in how you feel, let your provider know immediately. This medication can also severely affect your bone marrow, gastrointestinal tract, liver, lungs, skin, and kidneys. It is important to notify your provider of any new symptoms or side effects you are having.

Nausea and/or Vomiting

Talk to your care team so they can prescribe medications to help you manage [nausea and vomiting](#). In addition, dietary changes may help. Avoid things that may worsen the symptoms, such as heavy or greasy/fatty, spicy or acidic foods (lemons, tomatoes, oranges). Try antacids, (e.g. milk of magnesia, calcium tablets such as Tums), saltines, or ginger ale to lessen symptoms.

Call your doctor or nurse if you are unable to keep fluids down for more than 12 hours or if you feel lightheaded or dizzy at any time.

Diarrhea

Your oncology team can recommend medications to relieve [diarrhea](#). Also, try eating [low-fiber](#), bland foods, such as white rice and boiled or baked chicken. Avoid raw fruits, vegetables, whole grain breads, cereals, and seeds. Soluble fiber is found in some foods and absorbs fluid, which can help relieve diarrhea. Foods high in soluble fiber include: applesauce, bananas (ripe), canned fruit, orange sections, boiled potatoes, white rice, products made with white flour, oatmeal, cream of rice, cream of wheat, and farina. Drink 8-10 glasses of non-alcoholic, un-caffeinated fluid a day to prevent dehydration.

Low White Blood Cell Count (Leukopenia or Neutropenia)

White blood cells (WBC) are important for fighting infection. While receiving treatment, your [WBC count can drop](#), putting you at a higher risk of getting an infection. You should let your doctor or nurse know right away if you have a fever (temperature greater than 100.4°F or 38°C), sore throat or cold, shortness of breath, cough, burning with urination, or a sore that doesn't heal.

Tips to preventing infection:

- [Washing hands](#), both yours and your visitors, is the best way to prevent the spread of infection.

- Avoid large crowds and people who are sick (i.e.: those who have a cold, fever or cough or live with someone with these symptoms).
- When working in your yard, wear protective clothing including long pants and gloves.
- Do not handle pet waste.
- Keep all cuts or scratches clean.
- Shower or bath daily and perform frequent [mouth care](#).
- Do not cut cuticles or ingrown nails. You may wear nail polish, but not fake nails.
- Ask your oncology care team before scheduling dental appointments or procedures.
- Ask your oncology care team before you, or someone you live with has any vaccinations.

Low Red Blood Cell Count (Anemia)

Your red blood cells are responsible for carrying oxygen to the tissues in your body. When the [red cell count is low](#), you may feel tired or weak. You should let your oncology care team know if you experience any shortness of breath, difficulty breathing, or pain in your chest. If the count gets too low, you may receive a blood transfusion.

Low Platelet Count (Thrombocytopenia)

Platelets help your blood clot, so when the [count is low](#) you are at a higher risk of bleeding. Let your oncology care team know if you have any excess bruising or bleeding, including nose bleeds, bleeding gums, or blood in your urine or stool. If the platelet count becomes too low, you may receive a transfusion of platelets.

- Do not use a razor (an electric razor is fine).
- Avoid contact sports and activities that can result in injury or bleeding.
- Do not take aspirin (salicylic acid), non-steroidal, anti-inflammatory medications (NSAIDs) such as Motrin/Advil (ibuprofen), Aleve (naproxen), Celebrex (celecoxib) etc. as these can all increase the risk of bleeding. Please consult with your healthcare team regarding use of these agents and all over the counter medications/supplements while on therapy.
- Do not floss or use toothpicks and use a soft-bristle toothbrush to brush your teeth.

Mouth Sores (Mucositis)

Certain cancer treatments can cause [sores or soreness in your mouth](#) and/or throat. Notify your oncology care team if your mouth, tongue, inside of your cheek or throat becomes white, ulcerated or painful. Performing [regular mouth care](#) can help prevent or manage mouth sores. If mouth sores become painful, your doctor or nurse can recommend a pain reliever.

- Brush with a soft-bristle toothbrush or cotton swab twice a day.
- Avoid mouthwashes that contain alcohol. A baking soda and/or salt with warm water mouth rinse (2 level teaspoons of baking soda or 1 level teaspoon of salt in an eight ounce glass of warm water) is recommended 4 times daily.
- If your mouth becomes dry, eat moist foods, drink plenty of fluids (6-8 glasses), and suck on sugarless hard candy.
- Avoid smoking and chewing tobacco, drinking alcoholic beverages, and citrus juices.

Loss or Thinning of Scalp and Body Hair (Alopecia)

Your hair may become [thin, brittle, or may fall out](#). This typically begins two to three weeks after treatment starts. This hair loss can be all body hair, including pubic, underarm, legs/arms, eyelashes, and nose hairs. The use of scarves, wigs, hats, and hairpieces may help. Hair generally starts to regrow soon after treatment is completed. Remember your hair helps keep you warm in cold weather, so a hat is particularly important in cold

weather or to protect you from the sun.

Nail and Skin Changes

Your fingernails/toenails may become dark, brittle, or fall off. Keep your fingernails and toenails clean and dry. You may use nail polish, but do not wear fake nails (gels, acrylics, overlay). If any nails fall off, clean the nail bed well with soap and water and cover with a band aid.

You may notice dry skin or changes in the color or tone of your skin. Your skin may be more sensitive to the sun, which can result in severe sunburn or rash. Sun sensitivity can last even after chemotherapy is completed. Avoid the sun between 10-2pm, when it is strongest. Wear sunscreen (at least SPF 30 with UVA/UVB protection) every day and reapply when in the sun for extended periods of time); wear sunglasses with UVA/UVB protection, a hat, and long sleeves/pants to protect your skin and seek out shade whenever possible.

Secondary Malignancies

There is a very low risk of developing leukemia, sarcoma, lung cancer, or other types of cancer due to treatment with this medication, which can occur many years after treatment. This is most often associated with repeated treatments or high doses.

Kidney Problems

This medication can cause kidney problems, including an increased creatinine level, which your oncology care team may monitor for using blood tests. Notify your healthcare provider if you notice decreased urine output, blood in the urine, swelling in the ankles, or loss of appetite.

Tumor Lysis Syndrome

If there are a large amount of tumor cells in your body prior to treatment, you are at risk for tumor lysis syndrome. This happens when the tumor cells die too quickly and their waste overwhelms the body. You may be given a medication (allopurinol) and IV fluids to help prevent this. If you experience nausea, vomiting, diarrhea, or become lethargic (drowsy, sluggish), notify your oncology team right away. TLS can affect your kidney function. Your provider will monitor your kidney function with blood work. Notify your provider if you have little or no urine output.

Radiation Recall

Radiation recall is when the administration of a medication causes a skin reaction that looks like a sunburn (redness, swelling, soreness, peeling skin) in areas where radiation was previously given. Notify your oncology team if you notice this side effect. Treatment can include topical steroid ointments and a delay in your next chemotherapy dose.

Important but Less Common Side Effects

- **Lung Changes:** This medication can cause an opportunistic infection called pneumocystis pneumonia. This medication can also cause interstitial pneumonitis, particularly when high doses have been received. Interstitial pneumonitis can develop months to years after treatment is completed and may be more common in people with pre-existing lung conditions. Call your oncology care team right away if you have shortness of breath, cough, wheezing or difficulty breathing.
- **Liver Toxicity:** This medication can cause liver toxicity, which your oncology care team may monitor for using blood tests called liver function tests. Notify your healthcare provider if you notice yellowing of the skin or eyes, your urine appears dark or brown, or you have pain in your abdomen, as these can be signs of liver toxicity,
- **Eye Problems:** This medication can cause your eyes to become irritated or watery and you may be more sensitive to light. Notify your provider if you develop any eye changes.
- **Neurologic changes:** This medication can affect the nervous system, causing you to feel drowsy,

dizzy, or confused. Notify your provider if you are feeling different.

Sexual & Reproductive Concerns

This medication may affect your reproductive system, resulting in the menstrual cycle or sperm production becoming irregular or stopping permanently. Women may experience menopausal effects including hot flashes and [vaginal dryness](#). In addition, the desire for sex may decrease during treatment. You may want to consider sperm banking or egg harvesting if you may wish to have a child in the future. Discuss these options with your oncology team.

Exposure of an unborn child to this medication could cause birth defects, so you should not become pregnant or father a child while on this medication. Effective birth control is necessary during treatment and for at least 6 months after treatment for women and 3 months after treatment for men. Even if your menstrual cycle stops or you believe you are not producing sperm. You should not breastfeed while receiving this medication or for one week after your last dose.

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