

# Methotrexate, Cytarabine, Thiotepe, and Rituximab

**Care Team Contact Information:** \_\_\_\_\_

**Pharmacy Contact Information:** \_\_\_\_\_

**Diagnosis:** \_\_\_\_\_

- This treatment is often used for primary central nervous system (CNS) lymphoma (PCNSL), but it may also be used for other reasons.

**Goal of Treatment:** \_\_\_\_\_

- Treatment may continue for a certain time period, until it no longer works, or until side effects are no longer controlled.

## Treatment Regimen

This regimen is often called by the acronym: “MATRix”

- **M:** Methotrexate
- **A:** Cytarabine (Ara-C)
- **T:** Thiotepe
- **Rix:** Rituximab

Treatment Name	How the Treatment Works	How the Treatment is Given
Methotrexate (MEH-thoh-TREK-sayt)	Stops cancer cells from making the instructions they need to grow and multiply, causing the cells to die.	Infusion given into a vein.
Cytarabine (sy-TAYR-uh-been): Ara-C	Stops cancer cells from making the instructions they need to grow and multiply, causing the cells to die.	Infusion given into a vein.
Thiotepe (THY-oh-TEH-puh): Tepadina (teh-pah-DEE-nuh), Tepylute	Slows down or stops the growth of cancer cells by damaging the genetic material that cancer cells need to grow.	Infusion given into a vein.
Rituximab (rih-TUK-sih-mab): Rituxan (rih-TUK-sun), Riabni, Ruxience, Truxima	Helps your immune system find and attack cancer cells by targeting a specific protein on their surface.	Infusion given into a vein.

**Note:** Your care team may use rituximab and hyaluronidase (Rituxan Hycela) instead of rituximab. Rituximab and hyaluronidase is given as an injection under the skin into the stomach area (abdomen) over 5 to 7 minutes.

**Treatment Administration and Schedule:** Treatment is typically repeated every 3 weeks. This length of time is called a “cycle”.

## ☐ Option #1

### Cycle 1

- Rituximab is given on Days -5, 0, 16, and 21.
- Methotrexate is given on Day 1.
  - You will receive leucovorin every 6 hours starting 24 hours after the start of the methotrexate infusion. This will continue until you have cleared most of the methotrexate from your body.
- Cytarabine is given every 12 hours for 4 doses on Days 2 and 3.
- Thiotepe is given on Day 4.

Treatment Name	Cycle 1, Days																										
	-5	-4	-3	-2	-1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Rituximab	✓					✓																✓					✓
Methotrexate							✓																				
Cytarabine								✓	✓																		
								✓	✓																		
Thiotepa										✓																	

### Cycles 2 and 3

- Rituximab is given on Days 16 and 21.
- Methotrexate is given on Day 1.
  - You will receive leucovorin every 6 hours starting 24 hours after the start of the methotrexate infusion. This will continue until you have cleared most of the methotrexate from your body.
- Cytarabine is given every 12 hours for 4 doses on Days 2 and 3.
- Thiotepe is given on Day 4.

Treatment Name	Cycle 2, Days																					Next Cycle
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	
Rituximab																✓					✓	
Methotrexate	✓																					✓
Cytarabine		✓	✓																			
		✓	✓																			
Thiotepe				✓																		

## Cycle 4

- Methotrexate is given on Day 1.
  - You will receive leucovorin every 6 hours starting 24 hours after the start of the methotrexate infusion. This will continue until you have cleared most of the methotrexate from your body.
- Cytarabine is given every 12 hours for 4 doses on Days 2 and 3.
- Thiotepa is given on Day 4.

Treatment Name	Cycle 4, Days																				
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
Methotrexate	✓																				
Cytarabine		✓	✓																		
		✓	✓																		
Thiotepa				✓																	

## ☐ Option #2

## Cycles 1 to 4

- Rituximab is given on Day 1.
- Methotrexate is given on Day 1.
  - You will receive leucovorin every 6 hours starting 24 hours after the start of the methotrexate infusion. This will continue until you have cleared most of the methotrexate from your body.
- Cytarabine is given every 12 hours for 4 doses on Days 2 and 3.
- Thiotepa is given on Day 4.

Treatment Name	Cycle 1								Next Cycle
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	...	Day 21	Day1
Rituximab	✓								✓
Methotrexate	✓								✓
Cytarabine		✓	✓						
		✓	✓						
Thiotepa				✓					

**Appointments:** Appointments may include regular check-ups with your care team, treatment appointments, lab visits, and imaging tests. It's important to keep your appointments whenever you can. If you miss any appointments, call your care provider as soon as possible to reschedule your appointment.

Supportive Care to Prevent and Treat Side Effects

Description	Supportive Care Given at the Clinic or Hospital	Supportive Care Taken at Home
To help lower the risk of infusion-related reactions		
To help prevent or treat nausea and vomiting		
To help your body make white blood cells to fight infections		
To help reduce the risk of infection		
To help prevent eye problems		
Other		

## Common Side Effects

Side Effect	Important Information
<b>Infusion Reactions (Boxed Warning)</b>	<p>Description: Infusion reactions are common with rituximab and can sometimes be severe or life-threatening. Infusion reactions may also occur with methotrexate, cytarabine, and thiotepe.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> <li>Your care team may prescribe medicines before each infusion of rituximab to help decrease your risk for infusion reactions or to help make any infusion reaction less severe.</li> <li>You may be monitored for infusion reactions during each infusion of rituximab.</li> <li>Your care team may slow down or stop your infusion or completely stop treatment with rituximab if you have an infusion reaction.</li> </ul> <p>Get medical help right away if you develop any of the following symptoms of infusion reaction during or after an infusion of rituximab:</p> <ul style="list-style-type: none"> <li>Chills or shaking</li> <li>Itching, rash, or flushing</li> <li>Trouble breathing or wheezing; tongue swelling</li> <li>Dizziness or feeling faint</li> <li>Fever of 100.4°F (or 38°C) or higher</li> <li>Pain in your back or neck</li> </ul>
<b>Low White Blood Cell (WBC) Count and Increased Infection Risk (Boxed Warning)</b>	<p>Description: WBCs help protect the body against infections. If you have a low WBC count, you might have a higher risk of infection.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> <li>Wash your hands and bathe regularly.</li> <li>Avoid crowded places.</li> <li>Stay away from people who are sick.</li> <li>Your care team may prescribe a drug that promotes the growth of WBCs.</li> </ul> <p>Talk to your care team if you have:</p> <ul style="list-style-type: none"> <li>Fever of 100.4°F (38°C) or higher</li> <li>Chills</li> <li>Cough</li> <li>Shortness of breath</li> <li>Sore throat</li> </ul>
<b>Low Platelet Count (Boxed Warning)</b>	<p>Description: Platelets help the blood clot and heal wounds. If you have low platelet counts, you might have a higher risk of bruising and bleeding.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> <li>Blow your nose gently and avoid picking it.</li> <li>Brush your teeth gently with a soft toothbrush and maintain good oral hygiene.</li> <li>Use an electric razor for shaving and a nail file instead of nail clippers.</li> <li>Consult your care team or dentist before medical or dental procedures, as you may need to pause your medication.</li> </ul> <p>Talk to your care team if you have:</p> <ul style="list-style-type: none"> <li>Nosebleed lasting over 5 minutes despite pressure</li> <li>Cut that continues to bleed</li> <li>Significant gum bleeding when flossing or brushing</li> <li>Severe headaches</li> <li>Blood in your urine or stool</li> <li>Blood in your spit after a cough</li> </ul>

<b>Low Red Blood Cell (RBC) Count and Hemoglobin (Hgb) (Boxed Warning)</b>	<p>Description: RBCs and Hgb help bring oxygen to your body's tissues and take away carbon dioxide. If you have low RBC counts or Hgb, you might feel weak, tired, or look pale.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> <li>• Get 7 to 8 hours of sleep each night.</li> <li>• Avoid operating heavy machinery when tired.</li> <li>• Balance work and rest, staying active but resting when needed.</li> </ul> <p>Talk to your care team if you have:</p> <ul style="list-style-type: none"> <li>• Shortness of breath</li> <li>• Dizziness</li> <li>• Fast or abnormal heartbeats</li> <li>• Severe headache</li> </ul>
<b>Nausea and Vomiting (Boxed Warning)</b>	<p>Description: Nausea is an uncomfortable feeling in your stomach or the need to throw up. This may or may not cause vomiting.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> <li>• Eat smaller, more frequent meals.</li> <li>• Avoid fatty, fried, spicy, or highly sweet foods.</li> <li>• Eat bland foods at room temperature and drink clear liquids.</li> <li>• If you vomit, start with small amounts of water, broth, or other clear liquids when you are ready to eat again. If that stays down, then try soft foods (such as gelatin, plain cornstarch pudding, yogurt, strained soup, or strained cooked cereal). Slowly work up to eating solid food.</li> <li>• Your care team may prescribe medicine for these symptoms.</li> </ul> <p>Talk to your care team if you have:</p> <ul style="list-style-type: none"> <li>• Vomiting for more than 24 hours</li> <li>• Vomiting that's nonstop</li> <li>• Signs of dehydration (like feeling very thirsty, having a dry mouth, feeling dizzy, or having dark urine)</li> <li>• Blood or coffee-ground-like appearance in your vomit</li> <li>• Bad stomach pain that doesn't go away after vomiting</li> </ul>
<b>Diarrhea (Boxed Warning)</b>	<p>Description: Diarrhea is when you have loose, watery bowel movements more often than usual. The need to use the bathroom may occur urgently.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> <li>• Keep track of how many times you go to the bathroom each day.</li> <li>• Drink 8 to 10 glasses of water or other fluids every day, unless your care team tells you otherwise.</li> <li>• Eat small meals of mild, low-fiber foods like bananas, applesauce, potatoes, chicken, rice, and toast.</li> <li>• Avoid eating foods with high fiber (like raw vegetables, fruits, and whole grains), foods that cause gas (like broccoli and beans), dairy foods (like yogurt and milk), and spicy, fried, and greasy foods.</li> <li>• Your care team may recommend medicine (such as loperamide) for diarrhea.</li> </ul> <p>Talk to your care team if you have:</p> <ul style="list-style-type: none"> <li>• 4 or more bowel movements than normal in 24 hours</li> <li>• Dizziness or lightheadedness while having diarrhea</li> <li>• Bloody diarrhea</li> </ul>

<b>Liver Problems (Boxed Warning)</b>	<p>Description: Treatment can harm your liver. This may cause nausea, stomach pain, and bleeding or bruising. It can also turn your skin and eyes yellow and make your urine dark. Lab tests may be performed to monitor liver function.</p> <p>Talk to your care team if you have:</p> <ul style="list-style-type: none"><li>• Yellowing of your skin or the whites of your eyes</li><li>• Severe nausea or vomiting</li><li>• Pain on the right side of your stomach area (abdomen)</li><li>• Dark urine (tea colored)</li><li>• Bleeding or bruising more easily than normal</li></ul>
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## Select Rare Side Effects

Side Effect	Talk to Your Care Team if You Have Any of These Signs or Symptoms
<b>Neurologic Problems (Boxed Warning)</b>	<p>Cytarabine and thiotepa can cause serious neurologic problems that can be life-threatening and lead to death. Neurologic problems may happen days or weeks after you receive cytarabine and thiotepa.</p> <ul style="list-style-type: none"> <li>Headache</li> <li>Agitation, trouble staying awake, confusion or disorientation, seeing or hearing things that are not real (hallucinations)</li> <li>Trouble speaking, writing, thinking, remembering things, paying attention, or understanding things</li> <li>Problems walking, muscle weakness, shaking (tremors), loss of balance, or muscle spasms</li> <li>Numbness and tingling (feeling like "pins and needles")</li> <li>Burning, throbbing, or stabbing pain</li> <li>Changes in your handwriting</li> <li>Seizures</li> </ul>
<b>Severe Skin and Mouth Reactions (Boxed Warning)</b>	<p>Rituximab, methotrexate, and thiotepa can cause severe skin and mouth reactions. You should shower at least 2 times a day and change your bed sheets daily on the days that you receive thiotepa and for 48 hours your dose of thiotepa. Avoid topical creams or ointments during thiotepa therapy. Accidental thiotepa exposure can cause skin reactions. Wash skin thoroughly with soap and water and flush mucous membranes if skin, mucous membrane, or both contact occurs.</p> <ul style="list-style-type: none"> <li>Painful sores or ulcers on your skin, lips, or in your mouth</li> <li>Blisters</li> <li>Peeling skin</li> <li>Rash</li> <li>Pustules</li> </ul>
<b>Hepatitis B Virus (HBV) Reactivation (Boxed Warning)</b>	<p>Before you start treatment, your care team will do blood tests to check for HBV infection. If you have had hepatitis B or are a carrier of hepatitis B virus, receiving rituximab could cause the virus to become an active infection again. Hepatitis B reactivation may cause serious liver problems, including liver failure and death. You should not receive rituximab if you have active hepatitis B liver disease. Your care team will monitor you for hepatitis B infection during and for several months after you stop receiving rituximab.</p> <ul style="list-style-type: none"> <li>Worsening tiredness</li> <li>Yellowing of your skin or white part of your eyes</li> </ul>
<b>Progressive Multifocal Leukoencephalopathy (PML) (Boxed Warning)</b>	<p>PML is a rare, serious brain infection caused by a virus that can happen in people who receive rituximab. People with weakened immune systems can get PML. PML can result in death or severe disability. There is no known treatment, prevention, or cure for PML.</p> <ul style="list-style-type: none"> <li>Confusion</li> <li>Dizziness or loss of balance</li> <li>Difficulty walking or talking</li> <li>Decreased strength or weakness on one side of your body</li> <li>Vision problems</li> </ul>
<b>Lung Problems (Boxed Warning)</b>	<ul style="list-style-type: none"> <li>Cough</li> <li>Shortness of breath</li> <li>Chest pain</li> </ul>



<b>Kidney Problems (Boxed Warning)</b>	<ul style="list-style-type: none"> <li>Decrease in your amount of urine</li> <li>Blood in your urine</li> <li>Swelling of your ankles</li> <li>Loss of appetite</li> </ul>
<b>Tumor Lysis Syndrome (TLS) (Boxed Warning)</b>	<p>Tumor lysis happens when cancer cells break apart and flood your bloodstream with chemicals and toxins faster than your body can get rid of them. TLS is a group of conditions that affect your heart, kidneys, and muscles.</p> <ul style="list-style-type: none"> <li>Severe nausea, vomiting, or diarrhea</li> <li>Urinating smaller amounts or dark-colored urine</li> <li>Muscle cramps or twitching</li> <li>Rapid heartbeats or chest pain</li> <li>Confusion or weakness</li> <li>Seizures</li> </ul>
<b>Risk of New Cancers (Boxed Warning)</b>	<p>There is a risk of developing new cancers during or after treatment. Talk with your care team about this risk, and ask about the signs and symptoms of new cancers.</p>
Cytarabine Syndrome	<p>Cytarabine syndrome is a rare reaction to cytarabine. It typically happens 6 to 12 hours after a dose of cytarabine.</p> <ul style="list-style-type: none"> <li>Fever of 100.4°F (38°C) or higher</li> <li>Chills</li> <li>Muscle or bone pain</li> <li>Rash</li> <li>Eye swelling or irritation</li> </ul>
Eye Problems	<p>Cytarabine can cause eye problems. Your care team may prescribe corticosteroid eye drops to help prevent or reduce the chance of severe eye problems. Start these drops before your first dose of cytarabine and use them until your care team tells you to stop.</p> <ul style="list-style-type: none"> <li>Eye irritation</li> <li>Redness of the eye</li> <li>Eye pain</li> <li>Dry eyes</li> </ul>
Pancreas Problems	<ul style="list-style-type: none"> <li>Upper stomach pain that may spread to your back and get worse with eating</li> <li>Weight loss</li> <li>Nausea or vomiting</li> </ul>

**Before starting treatment, ask your care team when to call 9-1-1 or seek emergency help.**  
**If you experience any new, worsening, or uncontrolled side effects, contact your care team immediately.**

## Intimacy, Fertility, Pregnancy, and Breastfeeding

- Treatment may **change how you feel about intimacy and your body**. However, physical closeness—such as holding hands and hugging—remains safe. It is common to have questions about intimacy. If needed, talk to your care team for guidance.
- Treatment can affect your **ability to have children**. It may damage your reproductive organs or stop them from working. If you are worried about fertility, talk to your care team before starting treatment.
- Treatment may **harm an unborn baby**.
  - If you are able to become pregnant, take a pregnancy test before starting treatment.
  - Use an effective method of birth control:
    - During treatment with MATRix.
    - For 6 months after your last doses of methotrexate and thiotepe.
    - For 1 year after your last dose of rituximab.
  - If you think you might be pregnant or if you become pregnant, tell your care team right away.
  - If your partner(s) could become pregnant, use an effective method of birth control, such as condoms:
    - During treatment with MATRix.
    - For 3 months after your last dose of methotrexate.
    - For 1 year after your last dose of thiotepe.
- **Do NOT breastfeed:**
  - During treatment with MATRix.
  - For 1 week after your last dose of methotrexate.
  - For 6 months after your last dose of rituximab.

## Handling Body Fluids and Waste

Some drugs you receive may stay in your urine, stool, sweat, or vomit for many days after treatment. Because many cancer drugs are toxic, your body waste may also be dangerous to touch. To help protect yourself, your loved ones, and the environment, **follow these instructions** for at least **48 hours** after each dose of **methotrexate, cytarabine, and thiotepe**:

- People who are pregnant should avoid touching anything that may be soiled with body fluids from the patient.
- You can use your usual toilet. Always close the lid and flush to discard all waste. If you have a low-flow toilet, flush twice.
- If the toilet or seat is soiled with urine, stool, or vomit, clean the surface after each use before others use it.
- Wash your hands with soap and water for at least 20 seconds after using the toilet.
- If you need a bedpan, inform your caregiver so they can wear gloves and assist with cleanup. Wash the bedpan with soap and water daily.
- If you cannot control your bladder or bowels, use a disposable pad with a plastic back, a diaper, or a sheet to absorb waste.
- Wash any skin exposed to body waste with soap and water.
- Wash soiled linens or clothing separately from other laundry. If you don't have a washer, place them in a plastic bag until they can be washed.
- Wash your hands with soap and water after touching soiled linens or clothing.

## Additional Information

- **Tell your care team about all the medicines you take.**

This includes prescriptions, over-the-counter drugs, vitamins, and herbal products. Before starting any new medicine, supplement, or vaccine, ask your care team first.

- Do not take nonsteroidal anti-inflammatory drugs (NSAIDs) (such as ibuprofen or naproxen), proton pump inhibitors (PPIs) (such as omeprazole or pantoprazole), penicillins, trimethoprim-sulfamethoxazole (Bactrim), phenytoin, and some antivirals during treatment with methotrexate. These medicines may significantly increase methotrexate levels, increasing the chance of severe side effects.
- Do not take products that contain folic acid or folate analog products, for example, leucovorin or levoleucovorin, during treatment with methotrexate, unless your care team instructs you to take them.
- Do not receive live vaccines during your treatment with MATRix.

- **Your care team will monitor the level of methotrexate in your blood.**

If your methotrexate levels are too high, you will receive additional medicines to lower the levels.

- **This Patient Education Sheet may not describe all possible side effects.**

Call your healthcare provider for medical advice about side effects. You may report side effects to the FDA at 1-800-FDA-1088.

## Notes

Updated Date: February 10, 2026

Scan the QR code below to access this education sheet.



Important notice: The Association of Cancer Care Centers (ACCC), Hematology/Oncology Pharmacy Association (HOPA), Network for Collaborative Oncology Development & Advancement, Inc. (NCODA), and Oncology Nursing Society (ONS) have collaborated in gathering information for and developing this patient education guide. This guide represents a brief summary of the medication derived from information provided by the drug manufacturer and other resources.

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