

# Rituximab, Methotrexate, and Temozolomide

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

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

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

- This treatment is often used for primary central nervous system lymphoma (PCNSL).
- 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 treatment is often called by its acronyms: MRT, RMT, or MTR

### MRT

- **M: Methotrexate**
- **R: Rituximab**
- **T: Temozolomide**

### RMT

- **R: Rituximab**
- **M: Methotrexate**
- **T: Temozolomide**

### MTR

- **M: Methotrexate**
- **T: Temozolomide**
- **R: Rituximab**

Treatment Name	How the Treatment Works	How the Treatment is Given
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 into a vein (intravenous (IV) infusion).
Methotrexate (MEH-thoh-TREK-sayt)	Stops cancer cells from making the instructions they need to grow and multiply, causing the cells to die.	Infusion into a vein (intravenous (IV) infusion).
Temozolomide (teh-moh-ZOH-loh-mide): Temodar (TEH-moh-dar)	Slows down or stops the growth of cancer cells by damaging the genetic material that cancer cells need to grow.	Capsule(s) taken by mouth.

**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 (subcutaneous injection) into the stomach area (abdomen) over 5 to 7 minutes.

**Treatment Administration and Schedule:** Treatment is typically repeated every 2 weeks. This length of time is called a “cycle”.

- Methotrexate is given on Day 1.
  - Your care team will monitor the level of methotrexate in your blood.
  - You will get a medicine called leucovorin. It helps protect healthy cells from the strong effects of high-dose methotrexate, but it does not make the methotrexate less effective against cancer. 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. It’s important to take leucovorin as prescribed by your care team to help prevent severe side effects.
  - If your methotrexate levels are too high, you will receive additional medicines to lower the levels.
- Rituximab is given on Day 3.
- Temozolomide is taken by mouth on Days 7 to 11. Temozolomide is only taken on odd cycle numbers.

**Note:** Your treatment schedule may be different than the one described in this sheet. Talk with your care team about your exact treatment schedule.

### Odd Cycle Number

Treatment Name	Cycle 1														Next Cycle
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 1
<b>Treatment Given at the Hospital or Clinic</b>															
Methotrexate	✓														✓
Rituximab			✓												
<b>Treatment Taken at Home</b>															
Temozolomide							✓	✓	✓	✓	✓				

### Even Cycle Number

Treatment Name	Cycle 2														Next Cycle
	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14	Day 1
<b>Treatment Given at the Hospital or Clinic</b>															
Methotrexate	✓														✓
Rituximab			✓												
<b>Treatment Taken at Home</b>															
Temozolomide															

Your temozolomide dosing instructions:

- Temozolomide comes in 6 capsule strengths: 5 mg, 20 mg, 100 mg, 140 mg, 180 mg, 250 mg.
  - Your care team may prescribe more than 1 strength for you, so it is important that you understand how to take your medicine the right way. Be sure that you understand exactly how many capsules you need to take each day of your treatment, and what strengths to take. This may be different whenever you start a new cycle.
- Take each day's dose of temozolomide at one time, with a full glass of water.
- Take temozolomide at the same time each day.
- Take temozolomide the same way each time, either with food or without food.
  - To help reduce nausea and vomiting, try to take temozolomide on an empty stomach or at bedtime.
- Swallow temozolomide capsules whole with water. Do not open, chew, or dissolve the contents of the capsules.
- If you take too much temozolomide, call your care team or go to the nearest hospital emergency room right away.

## Storage and Handling of Temozolomide

- Store temozolomide at room temperature between 68°F and 77°F (20°C and 25°C).
- If temozolomide capsules are accidentally opened or damaged, be careful not to breathe in (inhale) the powder from the capsules or get the powder on your skin or mucous membranes (for example, in your nose or mouth). If contact with any of these areas happens, wash the area with water right away.
- Keep temozolomide and all medicines out of the reach of children and pets.
- Whenever possible, give temozolomide to yourself and follow the steps below. If someone else gives it to you, they must also follow these steps:
  1. Wash your hands with soap and water.
  2. Put on gloves to avoid touching the medication. Note: Gloves are not needed if you give the drug to yourself.
  3. Transfer the temozolomide from its package to a small medicine or other disposable cup.
  4. Administer the medicine immediately by mouth with water.
  5. Remove gloves, if used, and throw them and the medicine cup in the household trash.
  6. Wash your hands with soap and water.
- If you plan to use a daily pill box or pill reminder, contact your care team before using it.
  - When the box or reminder is empty, wash it with soap and water before refilling.
  - The person refilling the box or reminder should:
    - Wear gloves. Note: Gloves are not needed if you are refilling it yourself.
    - Wash their hands with soap and water after completing the task, regardless of whether gloves were worn.
- Ask your care team how to safely throw away any unused temozolomide. Do not throw it in the trash or flush it down the sink or toilet.

**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 reduce the risk of infusion-related reactions	<hr/> <hr/> <hr/> <hr/>	<hr/> <hr/> <hr/> <hr/>
To help prevent or treat nausea and vomiting	<hr/> <hr/> <hr/> <hr/>	<hr/> <hr/> <hr/> <hr/>
To help reduce the risk of infection	<hr/> <hr/> <hr/> <hr/>	<hr/> <hr/> <hr/> <hr/>
Other	<hr/> <hr/> <hr/> <hr/>	<hr/> <hr/> <hr/> <hr/>

Common Side Effects

Side Effect	Important Information
<p><b>Infusion-Related Reactions (Boxed Warning)</b></p>	<p>Description: An infusion reaction is a bad response that can happen during or shortly after receiving medicine through a vein.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> <li>• Your care team may prescribe medicines before your infusion 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.</li> <li>• Your care team may slow down or stop your infusion, or completely stop treatment if you have an infusion reaction.</li> </ul> <p>Get medical help right away if you develop any of the following during or after your infusion:</p> <ul style="list-style-type: none"> <li>• Chills or shaking</li> <li>• Itching, rash, or flushing</li> <li>• Trouble breathing, wheezing, or tongue swelling</li> <li>• Dizziness or feeling faint</li> <li>• Feeling of impending doom</li> <li>• Fever of 100.4°F (38°C) or higher</li> <li>• New or severe pain in your back or neck</li> </ul>
<p><b>Low White Blood Cell (WBC) Count (Neutropenia) and Increased Risk of Infection (Boxed Warning)</b></p>	<p>Description: WBCs help protect your body from infections. A low WBC count increases your risk of getting infections.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> <li>• Wash your hands often and bathe regularly.</li> <li>• Avoid crowded places and close contact with people who are sick.</li> <li>• Follow food safety and wound-care advice from your care team.</li> <li>• Your care team may prescribe medicine to help your WBCs recover.</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>• New or worsening cough or sore throat</li> <li>• Painful urination or signs of a urinary infection</li> <li>• Feeling much more tired than usual</li> <li>• Red, swollen, warm, or painful areas on the skin (possible skin infection)</li> </ul>
<p><b>Low Platelet Count (Thrombocytopenia) (Boxed Warning)</b></p>	<p>Description: Platelets help your blood clot and wounds heal. A low platelet count increases your 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 with a soft toothbrush and keep good oral hygiene.</li> <li>• Use an electric razor for shaving and a nail file instead of nail clippers.</li> <li>• Avoid over-the-counter medicines that can increase bleeding risk (for example, nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen).</li> <li>• Tell your care team or dentist before medical or dental procedures — you may need to pause treatment.</li> </ul> <p>Talk to your care team if you have:</p> <ul style="list-style-type: none"> <li>• A nosebleed lasting more than 5 minutes despite pressure</li> <li>• A cut that continues to bleed</li> <li>• Heavy gum bleeding when brushing or flossing</li> <li>• Severe or sudden headache</li> <li>• Blood in your urine or stool</li> <li>• Blood in your spit after coughing</li> </ul>

<p><b>Low Red Blood Cell (RBC) Count and Hemoglobin (Hgb) (Anemia) (Boxed Warning)</b></p>	<p>Description: RBCs and Hgb carry oxygen to your body's tissues and remove carbon dioxide. Low RBC or Hgb (anemia) can make you feel weak, very tired, or look pale.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> <li>• Aim for 7 to 8 hours of sleep each night.</li> <li>• Do not drive, operate heavy machinery, or do other dangerous activities if you are very tired.</li> <li>• Balance activity and rest — stay as active as you can, but rest when needed.</li> <li>• Eat a balanced diet and follow any nutrition or supplement advice from your care team.</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 or fainting</li> <li>• Fast or irregular heartbeats</li> <li>• Sudden or severe headache</li> </ul>
<p><b>Nausea and Vomiting (Boxed Warning)</b></p>	<p>Description: Nausea is an uncomfortable feeling in your stomach or the need to throw up. You may or may not vomit.</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 sips of water, broth, or other clear liquids. If these stay down, try soft foods (such as gelatin, plain cornstarch pudding, yogurt, strained soup, and strained cooked cereal) and slowly return to solid foods.</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>• Nonstop vomiting</li> <li>• Signs of dehydration (very thirsty, dry mouth, dizziness, or dark urine)</li> <li>• Blood or coffee-ground-like appearance in your vomit</li> <li>• Severe stomach pain that does not go away after vomiting</li> </ul>
<p><b>Diarrhea (Boxed Warning)</b></p>	<p>Description: Diarrhea is loose, watery stools or more frequent bowel movements than usual. It can cause dehydration and weakness.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> <li>• Keep track of how often you go to the bathroom each day.</li> <li>• Drink 8 to 10 glasses of water or other fluids daily, unless your care team tells you otherwise.</li> <li>• Eat small meals of mild, low-fiber foods (such as bananas, applesauce, potatoes, chicken, rice, toast).</li> <li>• Avoid high-fiber foods (such as raw vegetables, fruits, and whole grains), gas-producing foods (such as broccoli and beans), dairy (such as milk and yogurt), and spicy, fried, or greasy foods.</li> <li>• Your care team may recommend an antidiarrheal medicine such as loperamide (Imodium).</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>• Signs of dehydration (very thirsty, dry mouth, dizziness, or dark urine)</li> <li>• Bloody diarrhea</li> </ul>

## Liver Problems (Boxed Warning)

Description: Treatment can cause liver injury. Your care team may check your liver with blood tests before and during treatment.

Talk to your care team if you have:

- Yellowing of your skin or the white part of your eyes (jaundice)
- Severe nausea or vomiting
- Pain on the right side of your stomach area (abdomen)
- Dark, tea-colored urine
- Bleeding or bruising more easily than normal



## Select Rare Side Effects

Side Effect	Talk to Your Care Team if You Have Any of These Signs or Symptoms
<b>Severe Skin and Mouth Reactions (Boxed Warning)</b>	<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 having 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>

**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, 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 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, 6 months after your last doses of temozolomide and methotrexate, and for 12 months 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 is able to become pregnant, use an effective method of birth control—such as condoms—during treatment with rituximab, methotrexate, and temozolomide, and for 3 months after your last doses of temozolomide and methotrexate.
- **Do NOT breastfeed** during treatment, for 1 week after your last dose of temozolomide and methotrexate, and 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** and **temozolomide**: (Note: Rituximab does not require special handling of body fluids and waste.)

- 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.

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

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

## Notes

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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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