

Lenalidomide and Rituximab (R²)

Care Team Contact Information: _____

Pharmacy Contact Information: _____

Diagnosis: _____

- This treatment is often used for follicular lymphoma (FL) or marginal zone lymphoma (MZL). 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

Your treatment is called “R-squared”. You may see this written as “R²” or “R2”.

- Lenalidomide (Revlimid)
- Rituximab

Treatment Name	How the Treatment Works	How the Treatment is Given
Lenalidomide (leh-nuh-LIH-doh-mide): Revlimid (REV-lih-mid)	Boosts the immune system, cuts off the cancer's blood supply, and directly attacks the cancer cells.	Capsule taken by mouth.
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).

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 4 weeks. This length of time is called a “cycle”.

Cycle 1

- Rituximab is given every week.
- Lenalidomide is taken 1 time a day for 21 days, followed by 7 days off.

Treatment Name	Cycle 1, Days																						
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23-28
Treatment Given at the Clinic or Hospital																							
Rituximab	✓							✓							✓								✓
Treatment Taken at Home																							
Lenalidomide	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	1 Week Break

Cycles 2 to 5

- Rituximab is given every 4 weeks.
- Lenalidomide is taken 1 time a day for 21 days, followed by 7 days off.

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	22	23-28	1
Treatment Given at the Clinic or Hospital																								
Rituximab	✓																							✓
Treatment Taken at Home																								
Lenalidomide	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	1 Week Break	✓

Cycles 6 and Beyond

- Lenalidomide is taken 1 time a day for 21 days, followed by 7 days off.

Treatment Name	Cycle 4, Days																							Next Cycle
	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22-28	1	
Lenalidomide	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	✓	1 Week Break	✓

Lenalidomide Instructions

Your lenalidomide dosing instructions:

- Lenalidomide comes in 6 capsule strengths: 2.5 mg, 5 mg, 10 mg, 15 mg, 20 mg, and 25 mg.
- Your dose may differ, but lenalidomide is typically taken as 20 mg once daily for 21 days (3 weeks), followed by 7 days (1 week) off.
- Take lenalidomide 1 time a day, at about the same time each day.
- Swallow lenalidomide capsules whole with water. Do not open, break, or chew your capsules.
- Lenalidomide may be taken with or without food.
- If you miss a dose of lenalidomide and it has been less than 12 hours since your usual time, take it as soon as you remember. If it has been more than 12 hours, skip the missed dose. Do not take 2 doses at the same time.
- If you take too much lenalidomide, call your care team right away.

Storage and Handling of Lenalidomide

- Store lenalidomide at room temperature between 68°F to 77°F in a dry location away from light.
- Keep lenalidomide out of the reach of children and pets.
- Whenever possible, give lenalidomide to yourself and follow the steps below. If someone else gives it to you, they must also follow these steps:
 1. Wash 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 lenalidomide 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 medicine cup in household trash.
 6. Wash hands with soap and water.
- Do not open or break lenalidomide capsules or handle them any more than needed.
 - If powder from the lenalidomide capsule comes in contact with your skin, wash the skin right away with soap and water.
 - If powder from the lenalidomide capsule comes in contact with the inside of your eyes, nose, or mouth, flush well with 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 lenalidomide. 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 lower the risk of infusion-related reactions	<hr/> <hr/> <hr/> <hr/>	<hr/> <hr/> <hr/> <hr/>
To help lower the risk of blood clots	<hr/> <hr/> <hr/> <hr/>	<hr/> <hr/> <hr/> <hr/>
To help lower the risk of infections	<hr/> <hr/> <hr/> <hr/>	<hr/> <hr/> <hr/> <hr/>
To help prevent or treat nausea and vomiting	<hr/> <hr/> <hr/> <hr/>	<hr/> <hr/> <hr/> <hr/>
Other	<hr/> <hr/> <hr/> <hr/>	<hr/> <hr/> <hr/> <hr/>

Common Side Effects

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

<p>Low Red Blood Cell (RBC) Count and Hemoglobin (Hgb) (Anemia)</p>	<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"> • Get 7 to 8 hours of sleep each night. • Avoid operating heavy machinery when tired. • Balance work and rest, staying active but resting when needed. <p>Talk to your care team if you have:</p> <ul style="list-style-type: none"> • Shortness of breath • Dizziness • Fast or abnormal heartbeats • Severe headache
<p>Fatigue</p>	<p>Description: Fatigue is a constant and sometimes strong feeling of tiredness.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> • Routine exercise has been shown to decrease levels of fatigue. Work with your care team to find the right type of exercise for you. • Ask your family and friends for help with daily tasks and emotional support. • Try healthy ways to feel better, like meditation, writing in a journal, doing yoga, and using guided imagery to lower anxiety and feel good. • Make a regular sleep schedule and limit naps during the day so you can sleep better at night, aiming for 7 to 8 hours of sleep. • Don't use heavy machines or do things that need your full attention if you're very tired to avoid accidents. <p>Talk to your care team if you have:</p> <ul style="list-style-type: none"> • Tiredness that affects your daily life • Tiredness all the time, and it doesn't get better with rest • Dizziness and weakness, along with being tired
<p>Constipation</p>	<p>Description: Constipation means having a hard time passing stools or not going to the bathroom often. Your stools might feel hard and dry, which can make you uncomfortable or hurt.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> • Keep track of how many times you move your bowels every day. • Drink 8 to 10 glasses of water or other fluids each day, unless your care team tells you otherwise. • Exercise regularly. • Eat high-fiber foods like raw fruits and vegetables. • Your care team may recommend medicine (such as polyethylene glycol 3350 or senna) for constipation. <p>Talk to your care team if you have:</p> <ul style="list-style-type: none"> • Constipation that lasts 3 or more days • Constipation after 48 hours, even after using a laxative

<p>Diarrhea</p>	<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"> • Keep track of how many times you go to the bathroom each day. • Drink 8 to 10 glasses of water or other fluids every day, unless your care team tells you otherwise. • Eat small meals of mild, low-fiber foods like bananas, applesauce, potatoes, chicken, rice, and toast. • 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. • Your care team may recommend medicine (such as loperamide) for diarrhea. <p>Talk to your care team if you have:</p> <ul style="list-style-type: none"> • 4 or more bowel movements than normal in 24 hours • Dizziness or lightheadedness while having diarrhea • Bloody diarrhea
<p>Rash or Itchy Skin</p>	<p>Description: Rash or itchy skin can cause symptoms like redness, swelling, and varying bumps, such as small red spots, welts, or patches.</p> <p>Recommendations:</p> <ul style="list-style-type: none"> • Keep your skin moisturized with creams or lotions to reduce rash and itchiness; wear loose-fitting clothing. • Avoid perfumes and colognes, as they may worsen rash symptoms. • Limit time spent in heat to prevent worsening symptoms. • Avoid sun exposure, especially between 10 AM and 4 PM, to lower the risk of sunburn. • Wear long-sleeved clothing with UV protection and broad-brimmed hats. • Apply broad-spectrum sunscreen (UVA/UVB) with at least SPF 30 as directed. • Use lip balm that contains at least SPF 30. • Avoid tanning beds. • Your care team may recommend medicines for symptoms. <p>Talk to your care team if you have:</p> <ul style="list-style-type: none"> • Rash or itching that continues to worsen

Select Rare Side Effects

Side Effect	Talk to Your Care Team if You Have Any of These Signs or Symptoms		
Blood Clots (Boxed Warning)	Signs or symptoms of a blood clot in the lung, arm, or leg may include: <ul style="list-style-type: none"> • Shortness of breath • Chest pain • Arm or leg swelling 	Signs or symptoms of a heart attack may include: <ul style="list-style-type: none"> • Chest pain that may spread to the arms, neck, jaw, back, or stomach area (abdomen) • Feeling sweaty • Shortness of breath • Feeling sick or vomiting 	Signs or symptoms of stroke may include: <ul style="list-style-type: none"> • Sudden numbness or weakness, especially on one side of the body • Severe headache or confusion • Problems with vision, speech, or balance
Severe Skin and Mouth Reactions (Boxed Warning)	<ul style="list-style-type: none"> • Painful sores or ulcers on your skin, lips, or in your mouth • Blisters • Peeling skin • Rash • Pustules 		
Hepatitis B Virus (HBV) Reactivation (Boxed Warning)	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. <ul style="list-style-type: none"> • Worsening tiredness • Yellowing of your skin or white part of your eyes 		
Progressive Multifocal Leukoencephalopathy (PML) (Boxed Warning)	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. <ul style="list-style-type: none"> • Confusion • Dizziness or loss of balance • Difficulty walking or talking • Decreased strength or weakness on one side of your body • Vision problems 		
Tumor Lysis Syndrome (TLS)	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. <ul style="list-style-type: none"> • Severe nausea, vomiting, or diarrhea • Urinating smaller amounts or dark-colored urine • Muscle cramps or twitching • Rapid heartbeats or chest pain • Confusion or weakness • Seizures 		
Risk of New Cancers	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.		

**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 cause **birth defects (deformed babies) or death of an unborn baby**. If you are pregnant or plan to become pregnant, you must not take lenalidomide.

You must not get pregnant:

- For at least 4 weeks before starting lenalidomide.
- During treatment with R².
- For at least 4 weeks after stopping lenalidomide.
- For at least 12 months after your last dose of rituximab.

If you can become pregnant:

- You will have pregnancy tests weekly for 4 weeks, then every 4 weeks if your menstrual cycle is regular, or every 2 weeks if your menstrual cycle is irregular.
- If you miss your period or have unusual bleeding, you will need to have a pregnancy test and receive counseling.
- You must agree to use 2 acceptable forms of birth control at the same time, for at least 4 weeks before, while taking, during any breaks (interruptions) in your treatment, and for at least 4 weeks after stopping lenalidomide.
- Talk with your healthcare provider to find out about options for acceptable forms of birth control that you may use to prevent pregnancy before, during, and after treatment with lenalidomide.
- If you had unprotected sex or if you think your birth control has failed, stop taking lenalidomide immediately and call your healthcare provider right away.

If you become pregnant while taking lenalidomide, stop taking it right away and call your healthcare provider. If your healthcare provider is not available, you can call the REMS Call Center at 1-888-423-5436. Healthcare providers and patients should report all cases of pregnancy to:

- FDA MedWatch at 1-800-FDA-1088, and
- The Lenalidomide REMS program at 1-888-423-5436

There is a pregnancy exposure registry that monitors the outcomes of anyone who take lenalidomide during pregnancy, or if their partner takes lenalidomide and they are exposed during pregnancy. You can enroll in this registry by calling the Lenalidomide REMS program at the phone number listed above.

Intimacy, Pregnancy, and Breastfeeding (Continued)

Lenalidomide can pass into human semen:

- Even if you have had a vasectomy, you must always use a latex or synthetic condom during any sexual contact with anyone who is or can become pregnant while taking lenalidomide, during any breaks (interruptions) in your treatment with lenalidomide, and for up to 4 weeks after stopping lenalidomide.
- Do not have unprotected sexual contact with anyone who is or could become pregnant. Tell your healthcare provider if you do have unprotected sexual contact with anyone who is or could become pregnant.
- Do not donate sperm while taking lenalidomide, during any breaks (interruptions) in your treatment, and for up to 4 weeks after stopping lenalidomide. If anyone becomes pregnant with your sperm, the baby may be exposed to lenalidomide and may be born with birth defects.

If your partner becomes pregnant, you should call your healthcare provider right away.

- **Do NOT breastfeed** during treatment with R² 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 **lenalidomide**:

- 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 drive, operate heavy machinery, or do other dangerous activities** if you develop dizziness, confusion, tremors, sleepiness, or any other symptoms that impair consciousness until your signs and symptoms go away. These may be signs and symptoms of CRS or neurologic problems.
- **Before starting lenalidomide, read and agree to the Lenalidomide REMS program and sign the Patient-Physician Agreement Form.** For details, call 1-888-423-5436 or visit www.lenalidomiderems.com.
- **Only a 28-day supply of lenalidomide can be obtained from the pharmacy at one time.** It is not eligible for automatic refills.
- **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: March 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.

This guide does not cover all existing information related to the possible uses, directions, doses, precautions, warnings, interactions, adverse effects, or risks associated with this medication and should not substitute for the advice of a qualified healthcare professional. Provision of this guide is for informational purposes only and does not constitute or imply endorsement, recommendation, or favoring of this medication by ACCC, HOPA, NCODA, or ONS, who assume no liability for and cannot ensure the accuracy of the information presented. All decisions related to taking this medication should be made with the guidance and under the direction of a qualified healthcare professional.

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