

For the Patient: LYVENETOR

LY=LYmphoma (tumour group)

VENETO= venetoclax (VENCLEXTA®)

R= riTUXimab (RITUXAN®)

Uses:

- **LYVENETOR** is a drug treatment for patients who have received at least one therapy in the past for chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL).

How does it work?

- **LYVENETOR** is a combination of two drugs, venetoclax (ven et' oh klax) and rituximab (ri-TUX-i-mab)
- Venetoclax works by blocking the action of a certain protein in the body that helps cancer cells survive, which helps kill cancer cells.
- Rituximab is a monoclonal antibody, a type of protein designed to target and interfere with the growth of cancer cells .

Treatment plan:

- You will take venetoclax daily on a low dose which will gradually be increased over 5 weeks. After you reach the target dose, you will take venetoclax every day and be given rituximab every 4 weeks for 6 cycles. After that, you will continue on venetoclax for a maximum of 2 years from the first day of rituximab.

Timing	Drug	Duration
Weeks 1-5	Venetoclax	Daily
Cycles 1-6	Venetoclax	Daily
	Rituximab	Once every 4 weeks
After cycle 6	Venetoclax	Daily x 2 years from day 1 of Cycle 1

- Venetoclax is a tablet that you take by mouth. Make sure you understand the directions. You may be given tablets of more than one strength to make the right dose. You may need to stay in the hospital for a few days while your dose is being adjusted.

- Rituximab is a liquid that can be given by injection into a vein or injected under the skin (subcutaneously or SC).
- Tell your doctor if you have ever had an unusual or **allergic reaction** to venetoclax or rituximab before receiving these drugs.

Venetoclax

- You need to **drink 1.5-2 litres of fluids** (8 glasses) every day for at least the first 6 weeks, starting two days before taking the first dose of venetoclax. You need to drink this amount of fluid during the time when the dose of venetoclax is increased until the target dose is reached and during the first week with rituximab. Usually this takes 6 weeks, but it may take longer for some people. Let your doctor know if you are not able to drink this amount of fluids daily. It is especially important to keep up this fluid intake 2 days before the dose increase and on the day of the dose increase to help prevent a side effect known as tumour lysis syndrome (TLS).
- Your doctor will give you a prescription for **allopurinol**. It is important that you start taking it 3 days before you take your first dose of venetoclax. You need to take this every day while the dose of venetoclax is increased until the target dose is reached and during the first week with rituximab. Usually this takes 6 weeks but it may take longer for some people.
- Blood tests will be taken regularly during treatment, especially **before each dose increase of venetoclax and 6 hours and 24 hours after the first 2 dose levels** (20 mg and 50 mg). The dose and timing of your treatment may be changed based on the test results and/or other side effects. Some patients may need more blood tests. Refer to dosing schedule at the end of this handout for timing of doses and blood tests.
- **Do not take the second dose** of venetoclax, the first 2 dose levels (20 mg and 50 mg) until the pharmacist reviews your lab results and informs you to do so. It is recommended that you **take your dose at 6am** and have your **blood test done at noon** to allow time for your blood test results to be reviewed.
- **Do not increase your dose** until the pharmacist reviews your lab results and informs you to do so.
- **Take** venetoclax with food.
- Do not chew, crush, or break venetoclax tablets. **Swallow whole.**
- If you **miss a dose** of venetoclax, take it as soon as you can if it is within 12 hours of the missed dose. If it is more than 12 hours since your missed dose, skip the missed

dose and go back to your usual dosing times. Call your doctor during office hours if a dose is missed during the time period when you are increasing your dose

- If you **vomit** the dose of venetoclax, skip the missed dose and go back to your usual dosing time. Do not take any doses to make up for the missed dose. Call your doctor during office hours for advice as a medication to prevent nausea may be required for future doses.
- Other drugs such as digoxin (LANOXIN[®]), ketoconazole (NIZORAL[®]), clarithromycin (BIAXIN[®]), rifampin (RIFADIN[®]), and warfarin (COUMADIN[®]) may **interact** with venetoclax. Tell your doctor if you are taking these or any other drugs as you may need extra blood tests or your dose may need to be changed. Check with your doctor or pharmacist before you start or stop taking any other drugs.
- **Do not eat grapefruit, grapefruit juice, Seville oranges and starfruit** for the duration of your treatment, as these may interact with venetoclax.
- It is safe to drink small amounts of alcohol when you are taking venetoclax.
- Venetoclax may affect **fertility** in men. If you plan to have children, discuss this with your doctor before being treated with venetoclax.
- Venetoclax may damage sperm and may harm the baby if used during pregnancy. It is best to use **birth control** while being treated with venetoclax and for at least 30 days after stopping treatment. Tell your doctor right away if you or your partner becomes pregnant. Do not breastfeed during treatment.
- **Store** venetoclax tablets out of the reach of children, at room temperature, away from heat, light, and moisture.
- **Tell** doctors, dentists, and other health professionals that you are being treated with venetoclax before you receive any treatment from them.
- On days when you are receiving rituximab, make sure you continue to take venetoclax.
- **Changes in blood counts** Venetoclax may cause temporary changes in your blood counts. Your doctor will be following these changes carefully by performing blood tests. Adjustment of your treatment may be needed in certain circumstances.

Rituximab

- Tell your doctor if you have ever had an infection with hepatitis virus, human immunodeficiency virus (HIV or the virus that causes AIDS), tuberculosis, or any other chronic infection.

- A blood test may be taken before each treatment. The dose and timing of your chemotherapy may be changed based on the test results and/or other side effects.
- Tell your doctor if you are taking drugs that lower your blood pressure as you may need to skip the dose of your blood pressure drug on the day of your treatment.
- The drinking of alcohol (in small amounts) does not appear to affect the safety or usefulness of rituximab.
- Rituximab may damage sperm and may harm the baby if used during pregnancy. It is best to use birth control while being treated with rituximab and for 12 months after. Tell your doctor right away if you or your partner becomes pregnant. Do not breastfeed during treatment.
- Tell doctors, dentists, and other health professionals that you are being treated with rituximab before you receive any treatment from them

BLOOD COUNTS	MANAGEMENT
<p>Normal platelets help your blood to clot normally after an injury (e.g., cut). When the platelet count is low, you may be more likely to bruise or bleed.</p>	<p>To help prevent bleeding problems:</p> <ul style="list-style-type: none"> • Try not to bruise, cut, or burn yourself. • Clean your nose by blowing gently. Do not pick your nose. • Avoid constipation. • Brush your teeth gently with a soft toothbrush as your gums may bleed more easily. <p>Some medications such as ASA (e.g., ASPIRIN[®]) or ibuprofen (e.g., ADVIL[®]) may increase your risk of bleeding.</p> <ul style="list-style-type: none"> • Do not stop taking any medication that has been prescribed by your doctor (e.g., ASA for your heart). • For minor pain, try acetaminophen (e.g., TYLENOL[®]) first, but occasional use of ibuprofen may be acceptable.

BLOOD COUNTS	MANAGEMENT
<p>Normal white blood cells protect your body by fighting bacteria (germs) that cause infection. When they are low, you are at greater risk of having an infection.</p>	<p>To help prevent infection:</p> <ul style="list-style-type: none"> • Wash your hands often and always after using the bathroom. • Stay away from crowds and people who are sick. • Call your doctor <i>immediately</i> at the first sign of an infection such as fever (over 100°F or 38°C by an oral thermometer), chills, cough, or burning when you pass urine.

Side effects are listed in the following table in the order in which they may occur. Tips to help manage the side effects are included.

SIDE EFFECTS	MANAGEMENT
<p>At the start of treatment, when there may be a fast breakdown of cancer cells, tumour lysis syndrome (TLS) can occur. If this happens, you are at greater risk of having kidney damage and other serious side effects.</p>	<p>To help prevent TLS:</p> <ul style="list-style-type: none"> • Drink 1.5 to 2 L of water each day for the first 6 weeks (or longer if needed). Start 2 days before your first dose (8 glasses). • You will receive a prescription for allopurinol - to reduce your risk of TLS; start 3 days before the first dose of venetoclax and take it every day until the doctor tells you to stop (usually for about 6 weeks). • Blood tests will be done before and after some or all dose increases. Do not take your next dose until your doctor knows your blood test results and tells you it is safe to do so. • Call your doctor <i>immediately</i> if you have more than one of these symptoms: abdominal pain/nausea/vomiting, dark or cloudy urine, moodiness, restlessness, confusion, muscle/joint pain, or seizures.

SIDE EFFECTS	MANAGEMENT
<p>Nausea and vomiting may occur. Most people have little or no nausea.</p>	<p>You may be given a prescription for antinausea drug(s) to take at home. It is easier to prevent nausea than treat it once it has occurred, so follow directions closely.</p> <ul style="list-style-type: none"> • Drink plenty of fluids. • Eat and drink often in small amounts. <p>Try the ideas in <i>Practical Tips to Manage Nausea</i>.*</p>
<p>Allergic reactions commonly occur with rituximab. Signs of an allergic reaction may include flushing, rash, hives, itching, dizziness, swelling or breathing problems. These reactions can occur immediately after receiving rituximab. Reactions usually only occur with the first or second treatment</p>	<p>Tell your nurse if this happens while you are receiving rituximab or contact your oncologist immediately if this happens after you leave the clinic.</p>
<p>Fever and chills may sometimes occur shortly after treatment with rituximab. Fever should last no longer than 24 hours.</p>	<ul style="list-style-type: none"> • Take acetaminophen (e.g., TYLENOL®) every 4-6 hours, to a maximum of 4 g (4000 mg) per day. • Fever (over 100°F or 38°C by an oral thermometer) which occurs more than a few days after treatment may be a sign of an infection. Report this to your doctor immediately.
<p>Skin rashes may sometimes occur.</p>	<p>If itching is very irritating, call your doctor. Otherwise, be sure to mention it at your next visit.</p>
<p>Diarrhea may sometimes occur.</p>	<p>If diarrhea is a problem:</p> <ul style="list-style-type: none"> • Drink plenty of fluids. • Eat and drink often in small amounts. • Do not eat high fibre foods as outlined in <i>Food Choices to Help Manage Diarrhea</i>.*
<p>Constipation may sometimes occur.</p>	<ul style="list-style-type: none"> • Exercise if you can. • Drink plenty of fluids. • Try ideas in <i>Food Choices to Manage Constipation</i>.*

SIDE EFFECTS	MANAGEMENT
Headache may sometimes occur.	<ul style="list-style-type: none"> • Take acetaminophen (e.g., TYLENOL[®]) every 4-6 hours if needed, to a maximum of 4 g (4000 mg) per day. • Tell your doctor if your headache doesn't go away or if it is associated with seizures, confusion, or changes in your eyesight.
Muscle or joint pain may sometimes occur.	You may take acetaminophen (e.g., TYLENOL[®]) every 4-6 hours to a maximum of 4 g (4000 mg) per day for mild to moderate pain. Tell your doctor if the pain interferes with your activity.
Sugar control may sometimes be affected in diabetic patients.	Check your blood sugar regularly if you are diabetic.
Swelling of hands, feet, or lower legs may sometimes occur if your body retains extra fluid.	If swelling is a problem: <ul style="list-style-type: none"> • Elevate your feet when sitting. • Do not wear tight clothing.
Tiredness and lack of energy may sometimes occur.	<ul style="list-style-type: none"> • Do not drive a car or operate machinery if you are feeling tired. • Try the ideas in <i>Fatigue/Tiredness – Patient Handout</i> *
Hair loss does not occur with venetoclax and is rare with rituximab. If you lose hair, it will grow back once you stop treatment with rituximab. Colour and texture may change	If hair loss is a problem, refer to Resources for Hair Loss and Appearance Changes – Patient Handout.*

***Please ask your chemotherapy nurse or pharmacist for a copy.**

STOP TAKING VENETOCLAX AND SEE YOUR DOCTOR OR GET EMERGENCY HELP IMMEDIATELY IF YOU HAVE:

- Signs of **tumour lysis syndrome**, such as more than one of these symptoms: abdominal pain/nausea/vomiting, dark or cloudy urine, moodiness, restlessness, confusion, shortness of breath, irregular heartbeat, unusual tiredness, fever/chills, seizure or muscle/joint pain.
- Signs of an **infection** such as fever (over 100°F or 38°C by an oral thermometer), shaking chills; severe sore throat, productive cough (coughing up thick or green sputum); cloudy or foul smelling urine; painful, tender, or swollen red skin wounds or sores.
- Signs of an **allergic reaction** (rare) soon after a treatment including dizziness, fast heart beat, face swelling, or breathing problems

- **Seizures or loss of consciousness**, with or without **confusion, headache**, or **changes in eyesight**.
- **Memory loss, trouble thinking, difficulty walking or clumsiness, weakness** on one side of the body, or changes in mood.
- Signs of **bleeding problems** such as black, tarry stools; blood in urine; pinpoint red spots on skin; extensive bruising.
- Signs of **heart or lung problems** such as fast or uneven heartbeat, chest pain, chest pressure, shortness of breath or difficulty in breathing; swelling of feet or lower legs, or fainting.

SEE YOUR DOCTOR AS SOON AS POSSIBLE (DURING OFFICE HOURS) IF YOU HAVE:

- Signs of **anemia** such as unusual tiredness or weakness.
- Signs of **liver problems** such as yellow eyes or skin, white or clay-coloured stools.
- Signs of **kidney problems** such as lower back or side pain, swelling of feet or lower legs.
- Signs of **gout** such as joint pain.

CHECK WITH YOUR DOCTOR IF ANY OF THE FOLLOWING CONTINUE OR BOTHER YOU:

- Uncontrolled nausea, vomiting, or diarrhea.
- Headache, muscle or back pain
- Skin rash, itching, or blistering
- Loss of appetite
- Dizziness.
- Easy bruising or minor bleeding.
- For diabetic patients: uncontrolled blood sugars.

REPORT ADDITIONAL PROBLEMS TO YOUR DOCTOR

Recommended Venetoclax dosing schedule for LOW OR MEDIUM TLS risk patients

Week (Dose)	Day	Date	Instructions for low or medium TLS risk patients
	Day -3		Start allopurinol 300 mg daily for the first 6 weeks of treatment (or longer if needed)
	Day -2		Start drinking 1.5-2 L of fluids daily for the first 6 weeks of treatment (or longer if needed)
Week 1 (20 mg)	Day 1		Take first dose (20 mg) at 6 am
			Go for blood test at 12 noon
	Day 2		Do NOT take dose. Go for blood test at 8 am. Wait for phone call from pharmacist for instructions on whether or not to take day 2 dose (expect a call approximately 2-3 hours after lab work is completed).
			Take 20 mg dose ONLY IF ADVISED TO DO SO by pharmacist
	Day 3		Take 20 mg dose at 8 am
	Day 4		Take 20 mg dose at 8 am
	Day 5		Take 20 mg dose at 8 am
	Day 6		Take 20 mg dose at 8 am
	Day 7		Take 20 mg dose at 8 am
		Go for blood test before 12 noon. Wait for phone call from pharmacist for instructions on whether or not to take week 2 day 1 dose (50 mg) the next day	
Week 2 (50 mg)	Day 1		Take 50 mg dose at 6 am ONLY IF PREVIOUSLY ADVISED TO DO SO by pharmacist
			Go for blood test at 12 noon
	Day 2		Do NOT take dose. Go for blood test at 8 am. Wait for phone call from pharmacist for instructions on whether or not to take week 2 day 2 dose.
			Take 50 mg dose dose ONLY IF ADVISED TO DO SO by pharmacist
Day 3		Take 50 mg dose at 8 am	

Week (Dose)	Day	Date	Instructions for low or medium TLS risk patients continued
Week 2 (50 mg)	Day 4		Take 50 mg dose at 8 am
	Day 5		Take 50 mg dose at 8 am
	Day 6		Take 50 mg dose at 8 am
	Day 7		Take 50 mg dose at 8 am
			Go for blood test before 12 noon. Wait for phone call from pharmacist for instructions on whether or not to take week 3 day 1 dose (100 mg) the next day.
Week 3 (100 mg)	Day 1		Take 100 mg dose at 8 am ONLY IF PREVIOUSLY ADVISED TO DO SO by pharmacist
	Day 2		Take 100 mg dose at 8 am
	Day 3		Take 100 mg dose at 8 am
	Day 4		Take 100 mg dose at 8 am
	Day 5		Take 100 mg dose at 8 am
	Day 6		Take 100 mg dose at 8 am
	Day 7		Take 100 mg dose at 8 am
		Go for blood test before 12 noon. Wait for phone call from pharmacist for instructions on whether or not to take week 4 day 1 dose (200 mg) the next day.	
Week 4 (200mg)	Day 1		Take 200 mg dose at 8 am ONLY IF PREVIOUSLY ADVISED TO DO SO by pharmacist
	Day 2		Take 200 mg dose at 8 am
	Day 3		Take 200 mg dose at 8 am
	Day 4		Take 200 mg dose at 8 am
	Day 5		Take 200 mg dose at 8 am
	Day 6		Take 200 mg dose at 8 am

Week (Dose)	Day	Date	Instructions for low or medium TLS risk patients continued
Week 4 (200mg)	Day 7		Take 200 mg dose at 8 am. Starter pack should be finished. Ensure you have medication for week 5
			Go for blood test before 12 noon. Wait for phone call from pharmacist for instructions on whether or not to take week 5 day 1 dose (400 mg) the next day.
Week 5 (400mg)	Day 1		Take 400 mg dose at 8 am ONLY IF PREVIOUSLY ADVISED TO DO SO by pharmacist
	Day 2		Take 400 mg dose at 8 am
	Day 3		Take 400 mg dose at 8 am
	Day 4		Take 400 mg dose at 8 am
	Day 5		Take 400 mg dose at 8 am
	Day 6		Take 400 mg dose at 8 am
	Day 7 onwards		Take 400 mg dose at 8 am

Recommended Venetoclax dosing schedule for HIGH TLS risk patients

Week (Dose)	Day	Date	Instructions for high TLS risk patients
	Day -3		Start allopurinol 300 mg daily for the first 6 weeks of treatment (or longer if needed)
	Day -2		Start drinking 1.5-2 L of fluids daily for the first 6 weeks of treatment (or longer if needed)
Week 1 (20 mg)	Day 1		Go to hospital for admission, hydration and to take first dose of venetoclax when informed to do so
	Day 2		Take 20 mg dose when approved by ward . May go home if blood tests normal
	Day 3		Take 20 mg dose at 8 am
	Day 4		Take 20 mg dose at 8 am
	Day 5		Take 20 mg dose at 8 am
	Day 6		Take 20 mg dose at 8 am
	Day 7		Take 20 mg dose at 8am Go for blood test before 12 noon
Week 2 (50 mg)	Day 1		Do NOT take 50 mg dose. Go to hospital for admission and hydration.
			Take 50 mg dose when approved by ward
	Day 2		Take 50 mg dose when approved by ward . May go home if blood tests normal
	Day 3		Take 50 mg dose at 8 am
	Day 4		Take 50 mg dose at 8 am
	Day 5		Take 50 mg dose at 8 am
Day 6		Take 50 mg dose at 8 am	

Week (Dose)	Day	Date	Instructions for high TLS risk patients continued
Week 2 (50 mg)	Day 7		Take 50 mg dose at 8am
			Go for blood test before 12 noon. Wait for phone call from pharmacist for instructions on whether or not to take week 3 day 1 dose (100 mg) the next day (expect a call approximately 2-3 hours after blood test is completed).
Week 3 (100 mg)	Day 1		Take 100 mg dose at 6 am ONLY IF PREVIOUSLY ADVISED TO DO SO by pharmacist.
			Go for blood test at 12 noon
	Day 2		Do NOT take dose. Go for blood test at 8 am. Wait for phone call from pharmacist for instructions on whether or not to take week 3 day 2 dose
			Take 100mg dose ONLY IF ADVISED TO DO SO by pharmacist
	Day 3		Take 100 mg dose at 8 am
	Day 4		Take 100 mg dose at 8 am
	Day 5		Take 100 mg dose at 8 am
	Day 6		Take 100 mg dose at 8 am
Day 7		Take 100 mg dose at 8 am	
		Go for blood test before 12 noon. Wait for phone call from pharmacist for instructions on whether or not to take week 4 day 1 dose (200 mg) the next day	
Week 4 (200 mg)	Day1		Take 200 mg dose at 6 am ONLY IF PREVIOUSLY ADVISED TO DO SO by pharmacist
			Go for blood test at 12 noon
	Day 2		Do NOT take dose. Go for blood test at 8 am. Wait for phone call from pharmacist for instructions on whether or not to take week 4 day 2 dose
			Take 200 mg dose ONLY IF PREVIOUSLY ADVISED TO DO SO by pharmacist
Day 3		Take 200 mg dose at 8am	

Week (Dose)	Day	Date	Instructions for high TLS risk patients continued
	Day 4		Take 200 mg dose at 8am
	Day 5		Take 200 mg dose at 8am
	Day 6		Take 200 mg dose at 8am.
	Day 7		Take 200 mg dose at 8am. Starter pack should be finished. Ensure you have medication for week 5
Go for blood test before 12 noon. Wait for phone call from pharmacist for instructions on whether or not to take week 5 day 1 dose (400 mg) the next day			
Week 5 (400 mg)	Day 1		Take 400 mg dose at 6 am ONLY IF PREVIOUSLY ADVISED TO DO SO by pharmacist
			Go for blood test at 12 noon
	Day 2		Go for blood test at 8 am. Wait for phone call from pharmacist for instructions on whether or not to take week 5 day 2 dose
			Take 400 mg dose ONLY IF PREVIOUSLY ADVISED TO DO SO by pharmacist
	Day 3		Take 400 mg dose at 8 am
	Day 4		Take 400 mg dose at 8 am
	Day 5		Take 400 mg dose at 8 am
	Day 6		Take 400 mg dose at 8 am
	Day 7 onwards		Take 400 mg dose at 8 am