

## For the Patient: LYVENOB

**LY**=LYmphoma (tumour group)

**VEN**= venetoclax (VENCLEXTA®)

**OB**= oBINutuzumab (Gazyva®)

### Uses:

- LYVENOB is a drug treatment for patients who have chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL) who have not received treatment before and currently need treatment.

### How does it work?

- LYVENOB is a combination of two drugs, oBINutuzumab (oh bi nue tooz ue mab) and venetoclax (ven et' oh klax).
- Venetoclax works by blocking the action of a certain protein in the body that helps cancer cells survive, which helps kill cancer cells.
- oBINutuzumab is a monoclonal antibody, a type of protein designed to target and interfere with the growth of cancer cells.

### Treatment plan:

- oBINutuzumab is a clear liquid that is injected into a vein. Venetoclax is a tablet taken by mouth.
- Your treatment plan consists of several (up to 12) chemotherapy cycles. Cycle 1 is three weeks long, cycle 2 is five weeks and from cycle 3 onwards, is four weeks long. See Table 1 for schedule:

**Table 1: Treatment schedule:**

Cycle #	Day	oBINutuzumab IV	Venetoclax PO	Cycle length
1	1	100 mg		21 days (3 weeks)
	2	900 mg		
	8	1000 mg		
	15	1000 mg		
2	1		20 mg daily x 7 days	35 days (5 weeks)
	8	1000 mg	50 mg daily x 7 days	
	15		100 mg daily x 7 days	
	22		200 mg daily x 7 days	
	29		400 mg daily x 7 days	
3 to 6	1	1000 mg	400 mg daily x 28 days	28 days (4 weeks)
7 to 12	1		400 mg daily x 28 days	28 days (4 weeks)

- For Cycle 1, you will receive oBINutuzumab on days 1, 2, 8 and 15. The infusion will take about 4 to 5 hours on Days 1 and 2 as the nurse will increase the rate slowly and monitor you closely for any infusion reactions. After that, each infusion will take about 3.5 to 4 hours.
- On the first day of Cycle 2, you will start taking venetoclax every day by mouth on a low dose which will gradually be increased over 5 weeks. 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. After you reach the target dose, you will take venetoclax every day.
  - On Day 8 of Cycle 2, you will receive oBINutuzumab intravenously and continue to take venetoclax every day.
- For cycles 3 to 6, you will receive oBINutuzumab once every 4 weeks. Make sure you continue to take venetoclax every day.
- From cycles 7 to 12, you will take venetoclax every day without oBINutuzumab infusion.
- Tell your doctor if you have ever had an unusual or **allergic reaction** to oBINutuzumab or venetoclax before receiving these drugs.

### **OBINutuzumab**

- You need to **drink 1.5-2 litres of fluids** (8 glasses) every day for at least the first 8 weeks, starting two days before the first oBINutuzumab infusion. You need to drink

this amount of fluid every day until the dose of venetoclax is increased to the target dose (until Cycle 3 Day 1), 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 increases of venetoclax 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 your first infusion of oBINutuzumab. You need to take this every day until the target dose of venetoclax is reached (until Cycle 3 Day 1). Usually this takes 8 weeks but it may take longer for some people.
- A blood test **may** be taken before **your** treatment. The dose and timing of your treatment may change based on the test results and/or other side effects.
- The drinking of alcohol (in small amounts) does not appear to affect the safety or usefulness of oBINutuzumab.
- oBINutuzumab may damage sperm and may harm the baby if used during pregnancy. It is best to use birth control while being treated with oBINutuzumab and for 18 months after. Tell your doctor right away if you or your partner becomes pregnant. Do not breastfeed during treatment and for 18 months after your last dose of oBINutuzumab.
- Tell doctors, dentists, and other health professionals that you are being treated with oBINutuzumab before you receive any treatment from them

## Venetoclax

- 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 6 am** 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.
- **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.

BLOOD COUNTS	MANAGEMENT
<p>Normal platelets help your blood to clot normally after an injury (e.g., cut). <b>When the platelet count is low, you may be more likely to bruise or bleed.</b></p>	<p>To help prevent bleeding problems:</p> <ul style="list-style-type: none"> <li>• Try not to bruise, cut, or burn yourself.</li> <li>• Clean your nose by blowing gently. Do not pick your nose.</li> <li>• Avoid constipation.</li> <li>• Brush your teeth gently with a soft toothbrush as your gums may bleed more easily.</li> </ul> <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"> <li>• Do not stop taking any medication that has been prescribed by your doctor (e.g., <b>ASA for your heart</b>).</li> <li>• For minor pain, try acetaminophen (e.g., TYLENOL®) first, but occasional use of ibuprofen may be acceptable.</li> </ul>
<p>Normal white blood cells protect your body by fighting bacteria (germs) that cause infection. <b>When they are low, you are at greater risk of having an infection.</b></p>	<p>To help prevent infection:</p> <ul style="list-style-type: none"> <li>• Wash your hands often and always after using the bathroom.</li> <li>• Stay away from crowds and people who are sick.</li> <li>• Call your doctor <b>immediately</b> 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.</li> </ul>

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, <b>tumour lysis syndrome</b> (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"> <li>• Drink 1.5 to 2 L of water each day for the first 8 weeks (or longer if needed). Start 2 days before your first dose (8 glasses).</li> <li>• You will receive a prescription for <b>allopurinol</b> - to reduce your risk of TLS; start 3 days before the first infusion of oBINutuzumab and take it every day until the doctor tells you to stop (usually for about 8 weeks).</li> <li>• Blood tests will be done before and after some or all dose increases of venetoclax. <b>Do not take your next dose until your doctor knows your blood test results and tells you it is safe to do so.</b></li> <li>• Call your doctor <b>immediately</b> if you have <b>more than one</b> of these symptoms: abdominal pain/nausea/vomiting, dark or cloudy urine, moodiness, restlessness, confusion, muscle/joint pain, or seizures.</li> </ul>
<p><b>Nausea and vomiting</b> may occur. Most people have little or no nausea.</p>	<p>You may be given a prescription for anti-nausea drug(s) to take at home. <b>It is easier to prevent nausea than treat it once it has occurred</b>, so follow directions closely.</p> <ul style="list-style-type: none"> <li>• Drink plenty of fluids.</li> <li>• Eat and drink often in small amounts.</li> </ul> <p>Try the ideas in <i>Practical Tips to Manage Nausea</i>.*</p>
<p><b>Allergic reactions</b> commonly occur with oBINutuzumab. Signs of an allergic reaction may include flushing, dizziness, or breathing problems. These reactions can occur immediately or several hours after receiving oBINutuzumab and usually only with the first or second dose.</p>	<p>Tell your nurse if this happens while you are receiving obinutuzumab or seek medical attention <b>immediately</b> if this happens after you leave the clinic.</p>
<p><b>Fever and chills</b> may sometimes occur shortly after treatment with oBINutuzumab. Fever should last no longer than 24 hours.</p>	<ul style="list-style-type: none"> <li>• Take acetaminophen (e.g., <b>TYLENOL®</b>) every 4-6 hours, to a maximum of 4 g (4000 mg) per day.</li> <li>• 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 <b>immediately</b>.</li> </ul>

SIDE EFFECTS	MANAGEMENT
<b>Skin rashes</b> may sometimes occur.	If itching is very irritating, call your doctor. Otherwise, be sure to mention it at your next visit.
<b>Diarrhea</b> may sometimes occur.	If diarrhea is a problem: <ul style="list-style-type: none"> <li>• Drink plenty of fluids.</li> <li>• Eat and drink often in small amounts.</li> <li>• Do not eat high fibre foods as outlined in <i>Food Choices to Help Manage Diarrhea</i>.*</li> </ul>
<b>Constipation</b> may sometimes occur.	<ul style="list-style-type: none"> <li>• Exercise if you can.</li> <li>• Drink plenty of fluids.</li> <li>• Try ideas in <i>Food Choices to Manage Constipation</i>.*</li> </ul>
<b>Headache</b> may sometimes occur.	<ul style="list-style-type: none"> <li>• Take acetaminophen (e.g., TYLENOL®) every 4-6 hours if needed, to a maximum of 4 g (4000 mg) per day.</li> <li>• Tell your doctor if your headache doesn't go away or if it is associated with seizures, confusion, or changes in your eyesight.</li> </ul>
<b>Muscle or joint pain</b> 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.
<b>Sugar control</b> may sometimes be affected in diabetic patients.	Check your blood sugar regularly if you are diabetic.
<b>Swelling</b> 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"> <li>• Elevate your feet when sitting.</li> <li>• Do not wear tight clothing.</li> </ul>
<b>Tiredness</b> and lack of energy may sometimes occur.	<ul style="list-style-type: none"> <li>• Do not drive a car or operate machinery if you are feeling tired.</li> <li>• Try the ideas in <i>Fatigue/Tiredness – Patient Handout</i> *</li> </ul>
<b>Hair loss</b> does not occur with venetoclax and is rare with oBINutuzumab. If you lose hair, it will grow back once you stop treatment with oBINutuzumab. 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
- 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.
- **Memory loss, trouble thinking, difficulty walking or clumsiness, weakness** on one side of the body, or changes in mood.

**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.
- Signs of **skin changes** such as a new wart; a sore or reddish bump that bleeds or does not heal; a change in size, shape, or colour of a mole; or thick or rough scaly patches of skin.

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

- Headache or pain not controlled with acetaminophen (e.g., TYLENOL®).
- Constipation.
- Dizziness
- Easy bruising, minor bleeding, or frequent nosebleeds.
- Redness, swelling, pain, or sores on your lips, tongue, mouth, or throat.
- Skin rash or dry, itchy skin.
- Loss of appetite, changes in taste, upset stomach, or weight changes.
- Trouble sleeping.
- For diabetics: uncontrolled blood sugars.





**Recommended Venetoclax dosing schedule for LOW OR MEDIUM TLS risk patients**

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

Cycle Week (Dose)	Day	Date	Instructions for low or medium TLS risk patients continued
Cycle 2 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. <b>Wait for phone call from pharmacist for instructions on whether or not to take week 3 day 1 dose (100 mg) the next day.</b>
Cycle 2 Week 3 (100 mg)	Day 1		Take 100 mg dose at 8 am <b>ONLY IF PREVIOUSLY ADVISED TO DO SO</b> 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. <b>Wait for phone call from pharmacist for instructions on whether or not to take week 4 day 1 dose (200 mg) the next day.</b>			
Cycle 2 Week 4 (200mg)	Day 1		Take 200 mg dose at 8 am <b>ONLY IF PREVIOUSLY ADVISED TO DO SO</b> 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

Cycle Week (Dose)	Day	Date	Instructions for low or medium TLS risk patients continued
Cycle 2 Week 4  (200mg)	Day 6		Take 200 mg dose at 8 am
	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. <b>Wait for phone call from pharmacist for instructions on whether or not to take week 5 day 1 dose (400 mg) the next day.</b>
Cycle 2  Week 5  (400mg)	Day 1		Take 400 mg dose at 8 am <b>ONLY IF PREVIOUSLY ADVISED TO DO SO</b> 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		Take 400 mg dose at 8 am
Cycle 3 to Cycle 12  (400mg)	Day 1 onwards		Take 400mg dose at 8 am

**Recommended Venetoclax dosing schedule for HIGH TLS risk patients**

<b>Cycle Week (Dose)</b>	<b>Day</b>	<b>Date</b>	<b>Instructions for high TLS risk patients</b>
Cycle 1	Day -3		Start <b>allopurinol 300 mg daily</b> for the first 8 weeks of treatment (or longer if needed)
	Day -2		Start drinking <b>1.5-2 L of fluids daily</b> for the first 8 weeks of treatment (or longer if needed)
Cycle 2 Week 1 <b>(20 mg)</b>	Day 1		Go to hospital for admission, hydration and to take first dose of venetoclax <b>when informed to do so</b>
	Day 2		Take 20 mg dose <b>when approved by ward</b> . 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
Cycle 2 Week 2 <b>(50 mg)</b>	Day 1		<b>Do NOT</b> take 50 mg dose. Go to hospital for admission and hydration.
			Take 50 mg dose <b>when approved by ward</b>
	Day 2		Take 50 mg dose <b>when approved by ward</b> . 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	

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

Cycle Week (Dose)	Day	Date	Instructions for high TLS risk patients continued
Cycle 2 Week 4 (200 mg)	Day 3		Take 200 mg dose at 8am
	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 <b>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</b>
Cycle 2 Week 5 (400 mg)	Day 1		Take 400 mg dose at <b>6 am ONLY IF PREVIOUSLY ADVISED TO DO SO</b> by pharmacist
			Go for blood test at <b>12 noon</b>
	Day 2		Go for blood test at <b>8 am. Wait for phone call from pharmacist for instructions on whether or not to take week 5 day 2 dose</b>
			Take 400 mg dose <b>ONLY IF PREVIOUSLY ADVISED TO DO SO</b> 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	
Cycle 3 to Cycle 12 (400mg)	Day 1 onwards		Take 400mg dose at 8 am