PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

[Pr]VENCLEXTA®

venetoclax tablets

Read this carefully before you start taking **VENCLEXTA** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **VENCLEXTA**.

Serious Warnings and Precautions

VENCLEXTA should only be prescribed by a doctor who is experienced in the use of anti-cancer drugs.

VENCLEXTA is only available through specialty pharmacies and/or retail oncology pharmacies that are part of AbbVie's managed distribution program. The Starting Pack is meant for patients with Chronic Lymphocytic Leukemia (CLL).

VENCLEXTA can cause the following 2 serious side effects:

- Tumour lysis syndrome (TLS).

  To reduce your risk of TLS:

  - You will start taking VENCLEXTA at a low dose. Your dose will be increased slowly up to the full dose:
    - Each week for 5 weeks, if you are taking VENCLEXTA for your CLL.
    - Each day for 3 days, if you are taking VENCLEXTA with azacitidine for your Acute Myeloid Leukemia (AML).
    - Each day for 4 days, if you are taking VENCLEXTA with low-dose cytarabine for your AML.
  - If you have CLL, your doctor will do blood tests during the first 5 weeks to check for TLS.
  - If you have AML, your doctor will do blood tests during the first week to check for TLS.
  - You will need to drink plenty of water. You may need to receive intravenous fluids at an outpatient clinic or hospital on specific days during the first 5 weeks if you have CLL, or 3 to 4 days if you have AML. You will also receive other medicines before starting VENCLEXTA to reduce your risk of TLS.
  - Do not take any medicines that may have a strong interaction with VENCLEXTA.
- Sepsis (a blood infection in the entire body).

  Some patients need to go to the hospital or may die from sepsis. Your doctor will closely monitor and treat you.

What is VENCLEXTA used for?

Chronic Lymphocytic Leukemia (CLL):

VENCLEXTA is used to treat adults with CLL. It is taken:

- **with another drug called obinutuzumab.** This is used when CLL has not been treated before.

Or

- **with another drug called rituximab.** This is used when CLL has come back or has not responded to treatment.

Or

- **by itself** when CLL:
  - has a chromosome deletion and has come back or has not responded to treatment; or
  - has no chromosome deletion and other treatments are not available.

CLL is a type of cancer that affects the lymph nodes and white blood cells called "B lymphocytes". In CLL, unhealthy B lymphocytes multiply too quickly and live for too long. This causes there to be too many of them in the blood.

Acute Myeloid Leukemia (AML):

VENCLEXTA is used to treat adults with AML:

- whose disease has not been treated before, and
- who are at least 75 years of age or have medical conditions that prevent them from having other types of chemotherapy.

For these patients, VENCLEXTA is taken with another drug. This could be either azacitidine or low-dose cytarabine.

AML is a cancer of the bone marrow and the blood. It affects white blood cells that are not fully developed called myeloid blasts. In AML, there are changes in the myeloid blasts that stop them from becoming mature blood cells. These immature blasts build up in the bone marrow and blood. This blocks normal cells from being produced and causes there to be lower number of healthy blood cells.

How does VENCLEXTA work?

VENCLEXTA works by blocking a protein in the body called "BCL-2". This is a protein that helps cancer cells survive. Blocking this protein helps to kill and lower the number of cancer cells.

What are the ingredients in VENCLEXTA?

Medicinal ingredient: venetoclax

Non-medicinal ingredients: calcium phosphate dibasic, colloidal silicon dioxide, copovidone, iron oxide yellow, polyethylene glycol, polysorbate 80, polyvinyl alcohol, sodium stearyl fumarate, talc and titanium oxide

The 50 mg tablet also contains iron oxide black and iron oxide red.

VENCLEXTA comes in the following dosage forms:

Tablets: 10 mg, 50 mg, and 100 mg

Do not use VENCLEXTA if:

- you are allergic to venetoclax or to any of the other ingredients in VENCLEXTA or to any part of the container.
- you have CLL and are taking certain medicines when you start your treatment and during the time when your dose is gradually being increased (usually over 5 weeks). This is because these medicines may have a strong interaction with VENCLEXTA. Some of these medicines include:
  - clarithromycin, used for bacterial infections
  - itraconazole, ketoconazole, posaconazole or voriconazole, used for fungal infections
  - ritonavir, used for HIV infection

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take VENCLEXTA. Talk about any health conditions or problems you may have, including if you:

- have low levels of neutrophils (a type of white blood cell), which is called neutropenia
- have kidney or liver problems
- have any signs or symptoms of infection such as fever, chills, cough, feeling weak or confused, or a painful or burning feeling when passing urine
- have recently received or are scheduled to receive a vaccine

Other warnings you should know about:

Bleeding problems

If you are a patient with AML and are taking VENCLEXTA with azacitidine or low-dose cytarabine, you may be at higher risk for serious bleeding problems. These bleeding problems could lead to death. Your healthcare professional will monitor you for signs of bleeding problems.

Other cancers

During treatment with VENCLEXTA, a higher number of cases of certain types of non-melanoma skin cancer have been reported. Your healthcare professional will monitor you for the signs of skin cancer.

Tumour lysis syndrome

VENCLEXTA can cause a serious side effect called tumour lysis syndrome (TLS). TLS is caused by the fast breakdown of cancer cells. As cancer cells are destroyed, they release their contents, leading to high levels of certain chemicals (potassium, uric acid, phosphorus) and low levels of calcium in the blood. High or low levels of these chemicals can cause serious damage to your kidneys or other organs and may lead to death. TLS is most likely to occur in the first days or weeks of treatment with VENCLEXTA, as you increase your dose. It can also happen if you need to stop and restart your treatment.

If you have a higher number of cancer cells in your body, kidney problems, or an enlarged spleen, your risk for TLS may be higher. The changes in your blood that could lead to TLS may have no symptoms. Having your blood tested is important in order to treat and prevent TLS. The symptoms below can be associated with rapid cell death or TLS:

- fever
- chills
- nausea (feeling sick to your stomach)
- vomiting
- confusion
- shortness of breath
- seizure
- irregular heartbeat
- dark or cloudy urine
- unusual tiredness
- muscle pain
- joint discomfort

If you notice any of these, call your doctor or nurse right away.

If you have CLL:

- Your doctor will do tests to check your risk of getting TLS before you start taking VENCLEXTA. Your doctor will also do blood tests during your first 5 weeks of treatment to check for TLS. It is important to keep your scheduled appointments for blood tests.
- Your doctor will give you other medicines before starting and during treatment with VENCLEXTA to help reduce your risk of TLS.

- You will need to drink plenty of water when taking VENCLEXTA to help reduce your risk of getting TLS.
    - For patients with CLL, follow the instructions about drinking water in the Quick Start Guide and as labelled inside the weekly wallet blister packs.
- Your doctor may hospitalize you before you start VENCLEXTA to give intravenous (IV) fluids into your vein, do blood tests, and check for TLS.

If you have AML:

- Your doctor may hospitalize you before you start your treatment. You may remain in hospital until 24 hours after you have reached the full VENCLEXTA dose. This will allow your healthcare professional to:
    - make sure that you have enough water/fluids,
    - give you medicines to prevent the build-up of uric acid in your body, and
    - do blood tests before you start to take VENCLEXTA, while they increase your dose and when you start to take the full dose.

Adults 65 years of age and older:

Adults 65 years of age and older may be more likely to experience certain side effects when taking VENCLEXTA in combination with other medicinal products.

Children and adolescents less than 18 years of age:

It is not known if VENCLEXTA is safe or will work in children or adolescents less than 18 years of age.

Pregnancy, breastfeeding, birth control and fertility:

- VENCLEXTA should not be used during pregnancy. It may harm your unborn baby. Tell your doctor immediately if you become pregnant.
- Women who are able to become pregnant should have a pregnancy test before starting treatment with VENCLEXTA and should use effective birth control during treatment with VENCLEXTA and for at least 30 days after stopping treatment.
- Do not breastfeed while you are taking this medicine.
- VENCLEXTA may cause male infertility (low or no sperm count). This may affect your ability to father a child. Ask your doctor for advice before starting treatment with VENCLEXTA.

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with VENCLEXTA:

- some medicines used to treat fungal infections – like fluconazole, itraconazole, ketoconazole, posaconazole and voriconazole
- some medicines used to treat bacterial infections – like ciprofloxacin, clarithromycin, erythromycin, nafcillin and rifampin
- some medicines used to prevent seizures or to treat epilepsy – like carbamazepine and phenytoin
- some medicines used to treat HIV infection – like efavirenz, etravirine, and ritonavir
- some medicines used to treat high blood pressure or heart-related chest pain (angina) – like bosentan, captopril, carvedilol, diltiazem, felodipine, ranolazine and verapamil
- a medicine used to treat a sleep disorder (narcolepsy) known as modafinil
- some herbal medicines – like St John's wort and quercetin
- a blood thinner known as warfarin
- some medicines used to treat heart conditions – like amiodarone, digoxin, quinidine and ticagrelor
- an immunosuppressant drug known as cyclosporine
- DO NOT eat grapefruit (or drink its juice), Seville oranges (or marmalades) or starfruit while you are taking VENCLEXTA. These products may increase the amount of VENCLEXTA in your blood.

How to take VENCLEXTA:

- Always take VENCLEXTA exactly as your doctor tells you.
- Drink plenty of water when taking VENCLEXTA to help reduce your risk of getting TLS.
- Take the tablets with a meal and water at the same time each day.
- Swallow VENCLEXTA tablets whole. Do not chew, crush, or break the tablets.
- Your doses of VENCLEXTA may be lower in some cases, including if:
  - you have severe liver problems, or
  - you are taking certain medicines that can interact with VENCLEXTA.
- Your treatment may be interrupted or your dose lowered if you experience certain side effects.

For patients with CLL:

When starting VENCLEXTA:

- Read the Quick Start Guide that comes with your Starting Pack (which contains 4 weekly wallet blister packs).
- Drink 7 glasses of water each day (1.75 litres total). Start drinking this amount of water 2 days before your first dose. Continue to drink this amount each day. This is especially important on the 2 days leading up to your first dose and every time your dose is increased (days 1, 6 and 7 of each week). Follow the instructions about drinking water in the Quick Start Guide and as labelled inside the weekly wallet blister packs.
- Your doctor will do required blood testing prior to starting each week of the Starting Pack, as well as 6 to 8 hours and 24 hours after your first dose for each of the first 2 weeks of VENCLEXTA treatment. Do not take your next dose until your doctor knows the results of these blood tests and tells you it is safe to do so.
- Do not start a new dose unless your doctor tells you it is safe to do so.

Usual dose:

Your doctor will start VENCLEXTA at a low dose for 1 week. Your doctor will gradually increase the dose over the next 4 weeks to the full standard dose.

The usual dose is as follows:

- The starting dose is 20 mg (two 10 mg tablets) once a day for 7 days.
- The dose will be increased to 50 mg (one 50 mg tablet) once a day for 7 days.
- The dose will be increased to 100 mg (one 100 mg tablet) once a day for 7 days.
- The dose will be increased to 200 mg (two 100 mg tablets) once a day for 7 days.
- The dose will be increased to 400 mg (four 100 mg tablets) once a day.
    - If you are taking VENCLEXTA alone, you will stay on the 400 mg daily dose, which is the standard dose, for as long as necessary.
    - If you are taking VENCLEXTA in combination with rituximab:
        - You will start your rituximab after the first 5 weeks of VENCLEXTA.
        - You will receive VENCLEXTA for 2 years.
    - If you are taking VENCLEXTA in combination with obinutuzumab:
        - You will start VENCLEXTA dosing after receiving your first cycle of obinutuzumab doses.
        - You will receive VENCLEXTA for 12 months.

For patients with AML:

- Your healthcare professional will do blood tests before you start taking VENCLEXTA. Blood tests will be repeated regularly throughout your treatment.
- Your healthcare professional will ensure that you are well hydrated during the time when your dose is being increased. They may also give you other medicines to help prevent side effects during this time.

Usual dose for VENCLEXTA in combination with azacitidine:

Your doctor will start VENCLEXTA at a low dose. Your doctor will gradually increase the dose over the next 3 days to the full dose.

The usual dose is as follows:

- The starting dose is 100 mg (one 100 mg tablet) once a day for 1 day.
- The dose will be increased to 200 mg (two 100 mg tablets) once a day for 1 day.
- The dose will be increased to 400 mg (four 100 mg tablets) once a day for 1 day.
- You will continue to take 400 mg (four 100 mg tablets) per day for as long as necessary. This is the standard dose.

You will start your azacitidine on the same day that you start VENCLEXTA.

Usual dose for VENCLEXTA in combination with low-dose cytarabine:

Your doctor will start VENCLEXTA at a low dose. Your doctor will gradually increase the dose over the next 4 days to the full dose.

The usual dose is as follows:

- The starting dose is 100 mg (one 100 mg tablet) once a day for 1 day.
- The dose will be increased to 200 mg (two 100 mg tablets) once a day for 1 day.
- The dose will be increased to 400 mg (four 100 mg tablets) once a day for 1 day.
- The dose will be increased to 600 mg (six 100 mg tablets) once a day.
- You will continue to take 600 mg (six 100 mg tablets) per day for as long as necessary. This is the standard dose.

You will start your cytarabine on the same day that you start VENCLEXTA.

If you have questions about your dose of VENCLEXTA, talk to your healthcare professional.

Overdose:

If you think you have taken too much VENCLEXTA, contact your healthcare professional, hospital emergency department or regional poison control centre immediately, even if there are no symptoms.

Missed dose:

- If it has been less than 8 hours, take your dose as soon as possible.
- If it has been more than 8 hours, skip the missed dose and take the next dose at your usual time the next day.
- If you vomit after taking VENCLEXTA, do not take an extra dose. Take the next dose at your usual time the next day.
- If you are not sure, talk to your healthcare professional.

What are possible side effects from using VENCLEXTA?

These are not all the possible side effects you may feel when taking VENCLEXTA. If you experience any side effects not listed here, contact your healthcare professional.

- diarrhea or constipation
- nausea
- vomiting
- decreased appetite
- weight loss
- stomach pain
- swelling of your arms, legs, hands and feet
- weakness
- mouth sores
- shortness of breath
- rash
- fever
- headache
- dizziness
- feeling tired

- cough
- muscle, back, bone, neck and joint pain
- itching

VENCLEXTA may cause abnormal exam and blood test results. Your doctor will do some tests before and during your treatment. The doctor will interpret the results. They will tell you if there are any abnormalities in your tests that might need treatment.

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
VERY COMMON			
Leukopenia, Neutropenia, Lymphopenia (low levels of white blood cells): any signs of infection such as fever, chills, sweating, aches, pains, fatigue and flu-like symptoms		✓	
Anemia (low levels of red blood cells): fatigue, pale skin, shortness of breath, weakness		✓	
Thrombocytopenia (low levels of blood platelets): increases risk of bleeding or bruising		✓	
Sepsis and septic shock (a blood infection in the entire body): fever or dizziness, chills, high or very low body temperature, feel weak, little or no urine, low blood pressure, palpitations, rapid breathing, rapid heartbeat			✓
COMMON			
Hemorrhage (bleeding problems): blood in stool, urine or eyes; vomiting blood; sudden and severe headache; nose bleeds; coughing up blood; purple spotted rash on the skin			✓
Hyperkalemia (high potassium levels in the blood): muscle fatigue, weakness, irregular heartbeat, nausea		✓	

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
Hypotension (low blood pressure): dizziness, fainting, light-headedness, blurred vision, nausea, vomiting, fatigue (may occur when you go from lying or sitting to standing up)		✓	
Pneumonia (infection of the lungs): chills, cough with or without mucus, fever, shortness of breath		✓	
Respiratory tract infection: runny nose, sore and scratchy throat, cough, sneezing, weak or loss of voice		✓	
Urinary tract infection: burning sensation during urination, low urine output despite feeling urge to urinate more often, pain in the pelvis or lower back, cloudy urine that may contain blood		✓	
RARE			
Tumour lysis syndrome (TLS): chills, confusion, dark or cloudy urine, fever, irregular heartbeat, joint discomfort, muscle pain, nausea, shortness of breath, seizure, tiredness, vomiting			✓
Multi-organ Dysfunction Syndrome (failure of multiple organs): failure of multiple organs (e.g., lung, kidney, heart) at the same time including passing less urine, difficulty breathing (including shortness of breath at rest or with activity), rapid breathing, wheezing or cough; yellowing of your skin and eyes, stomach pain or swelling, nausea or vomiting; chest pain (angina), shortness of breath, rapid, strong or irregular heartbeat, or if there is swelling of your ankles or feet			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, talk to your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

Store between 2 and 30°C.

Keep out of reach and sight of children.

Access to VENCLEXTA

VENCLEXTA is only available through specialty pharmacies and/or retail oncology pharmacies that are part of AbbVie's managed distribution program. Talk to your doctor for more information.

If you want more information about VENCLEXTA:

- Talk to your healthcare professional.
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html), the manufacturer's website (www.abbvie.ca), or by calling 1-888-704-8271.

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