PATIENT INFORMATION LEAFLET

VENCLEXTA™ TABLET

1. What is in this leaflet.

This leaflet contains important information about the safe and effective use of this medicine. Read the entire leaflet carefully before you start taking this medicine.

2. What the most important information is.

VENCLEXTA can cause tumor lysis syndrome (TLS), a serious side effect that can lead to death. 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 kidneys and other organs and may lead to sudden kidney failure or death. 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 heart beat
- dark or cloudy urine
- unusual tiredness
- muscle pain
- joint discomfort

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

TLS is most likely to occur when you are first starting your treatment.

Before you start VENCLEXTA your doctor will do blood tests and a scan (for example, a CT scan if you have CLL) to determine your risk of TLS. It is important to keep your scheduled appointments for blood tests.

To help prevent TLS, it is important to stay hydrated and drink water every day when taking VENCLEXTA. Particularly, starting 2 days before and on the day of your first dose of VENCLEXTA, and every time the dose is increased, drink 6-8 glasses (approximately 56 ounces/1.5 – 2 liters total) of water each day.

Your doctor may give you medicine to help prevent TLS.

Your doctor may hospitalize you before you start VENCLEXTA to give intravenous (IV) fluids into your vein, do blood tests, and check for TLS.

3. What VENCLEXTA is taken for.

VENCLEXTA is taken in combination with obinutuzumab to treat patients with chronic lymphocytic leukemia (CLL) that has not been treated before.

VENCLEXTA is taken, in combination with rituximab or alone, to treat patients with CLL when the disease comes back after it has been treated.

- CLL is a type of cancer affecting white blood cells called "B lymphocytes" and the lymph nodes. In CLL, the B lymphocytes multiply too quickly and live for too long, so that there are too many of them in the blood.

VENCLEXTA is taken, in combination with a hypomethylating agent or with low-dose cytarabine, to treat acute myeloid leukemia (AML) in people who were previously not treated and who are not eligible for intensive chemotherapy.

- AML is a cancer of the myeloid precursor blood cells (myeloid blasts). Changes in these cells stop myeloid blasts from becoming mature blood cells. As a result, there is a buildup of immature blasts in the marrow and blood. In turn, there are too few red blood cells, platelets, and granulocytes (type of white blood cell).

4. What VENCLEXTA does.

The active substance in this medicine is called venetoclax.

VENCLEXTA belongs to a group of medicines called BCL-2 inhibitors.

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. It also slows down the worsening of the disease.

5. When you must not take VENCLEXTA.

Do not take VENCLEXTA if you are taking certain other medicines listed in Section 7.

6. What you need to know about taking VENCLEXTA.

Before you take VENCLEXTA, tell your doctor if:
- You have kidney or liver problems
- You have an infection
- You have recently received or are scheduled to receive a vaccine
- You are pregnant or plan to become pregnant
- You are breastfeeding or plan to breastfeed

Once you have started VENCLEXTA, tell your doctor if you experience:
- Symptoms of TLS, listed in Section 2
- Symptoms of infection, listed in Section 10

7. Taking other medicines with VENCLEXTA.

When you start treatment and during the time when the dose is gradually increased, serious or life-threatening effects can occur when VENCLEXTA is taken with certain medicines. Do not take VENCLEXTA and talk to your doctor if you are taking any of the following:
- itraconazole, ketoconazole, posaconazole, or voriconazole, for fungal infections
- clarithromycin for bacterial infections
- ritonavir for HIV infection

Tell your doctor if you are taking any of the medicines listed below. Your doctor may need to change the dose of VENCLEXTA.

Certain medicines and supplements may increase or decrease the amount of VENCLEXTA in your blood, including:
- medicines for fungal infections – itraconazole, fluconazole, ketoconazole, posaconazole, or voriconazole
- medicines called antibiotics to treat bacterial infections – ciprofloxacin, clarithromycin, erythromycin, nafcillin, or rifampicin
- medicines to prevent seizures or to treat epilepsy – carbamazepine, phenytoin
- medicines for HIV infection – efavirenz, etravirine, ritonavir
- medicines to treat blood pressure or angina – bosentan, diltiazem, verapamil
- a medicine to treat a sleep disorder (narcolepsy) known as modafinil
- an herbal medicine known as St. John's wort

VENCLEXTA may affect the way other medicines work, including:
- a blood thinner known as warfarin
- a heart failure medicine known as digoxin

8. Pregnancy, contraception, breastfeeding, and fertility with VENCLEXTA.

Pregnancy

VENCLEXTA should not be used during pregnancy. There is no information about the safety of VENCLEXTA in pregnant women. Tell your doctor immediately if you become pregnant.

Contraception

Women who are able to become pregnant should use effective birth control (contraception) during treatment with VENCLEXTA and for at least 30 days after stopping treatment.

Breastfeeding

Do not breastfeed while you are taking this medicine.

Fertility

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.

9. Driving and using machines with VENCLEXTA.

It is not known if VENCLEXTA affects the ability to drive or use machines.

10. Possible side effects with VENCLEXTA.

VENCLEXTA can cause serious side effects, including:

Tumor Lysis Syndrome: See "What the most important information is" for information about TLS.

Low white blood cell count (neutropenia; very common) (may affect more than 1 in 10 people)**:** Your doctor will check your blood count during treatment with VENCLEXTA. Low white blood cell count can increase your risk for infection. Signs of infection may include:

- fever
- chills
- feeling weak or confused
- cough
- pain or burning feeling when passing urine

Some infections can be serious and may lead to death. Tell your doctor immediately if you have signs of an infection while taking VENCLEXTA.

The following side effects may happen with this medicine:

<u>For patients with CLL:</u>

Very common (may affect more than 1 in 10 people)

- upper respiratory tract infection – signs include runny nose, sore throat, or cough
- diarrhea
- feeling or being sick (nausea or vomiting)
- constipation
- feeling tired

Blood tests may also show

- lower number of red blood cells
- higher level of a body salt (electrolyte) called phosphate

Common (may affect up to 1 in 10 people)
- severe infection in the blood (sepsis)
- pneumonia
- urinary tract infection
- low number of white blood cells with fever (febrile neutropenia)

Blood tests may also show
- higher level of creatinine
- higher level of urea
- higher level of potassium
- lower level of calcium
- lower number of white blood cells called lymphocytes

For patients with AML:

Very common (may affect more than 1 in 10 people)
- feeling or being sick (nausea or vomiting)
- diarrhea
- mouth sores
- feeling tired or weak
- infection of lung or blood
- decreased appetite
- joint pain
- dizziness or fainting
- headache
- shortness of breath
- bleeding
- low blood pressure
- urinary tract infection
- weight loss
- pain in belly (abdominal pain)

Blood tests may also show
- lower number of platelets (thrombocytopenia)
- lower number of white blood cells with fever (febrile neutropenia)
- lower number of red blood cells (anemia)
- higher level of total bilirubin
- low level of potassium in the blood

Common (may affect up to 1 in 10 people)
- gall stones or gall bladder infection
- tumor lysis syndrome

11. How VENCLEXTA is administered.

How much VENCLEXTA to take

Always take VENCLEXTA exactly as your doctor tells you.

If you are taking certain medications that can interact with VENCLEXTA, your doctor may choose to reduce the starting dose. Notify your doctor of any medications that you are, or might be, taking.

For patients with CLL:

You will begin treatment with VENCLEXTA at a low dose for 1 week. Your doctor will gradually increase the dose over the next four weeks to the full standard dose.

- The starting dose is 20 mg (two 10 mg tablets) once a day for 7 days.
- The dose will be increased to 50 mg once a day for 7 days.
- The dose will be increased to 100 mg once a day for 7 days.
- The dose will be increased to 200 mg once a day for 7 days.
- The dose will be increased to 400 mg once a day.
    - When you are receiving VENCLEXTA therapy alone, you will stay on the 400 mg daily dose, which is the standard dose, for as long as necessary.
    - When you are receiving VENCLEXTA therapy in combination with rituximab, you will receive the 400 mg daily dose for 24 months.
    - When you are receiving VENCLEXTA therapy in combination with obinutuzumab, you will receive the 400 mg daily dose for approximately 10 months.

For patients with AML taking VENCLEXTA in combination with azacitidine or decitabine:

You will begin treatment with VENCLEXTA at a low dose. Your doctor will gradually increase the dose over the next 3 days to the full standard dose.

- The starting dose is 100 mg once a day for 1 day.
- The dose will be increased to 200 mg once a day for 1 day.
- The dose will be increased to 400 mg once a day. You will stay on the 400 mg daily dose, which is the standard dose, for as long as necessary.

For patients with AML taking VENCLEXTA in combination with low-dose cytarabine:

You will begin treatment with VENCLEXTA at a low dose. Your doctor will gradually increase the dose over the next 4 days to the full standard dose.

- The starting dose is 100 mg once a day for 1 day.
- The dose will be increased to 200 mg once a day for 1 day.
- The dose will be increased to 400 mg once a day for 1 day.

• The dose will be increased to 600 mg once a day. You will stay on the 600 mg daily dose, which is the standard dose, for as long as necessary.

How to take

- Take the tablets by mouth (orally).
- Take the tablets with a meal and water at approximately the same time each day.
- Do not chew, crush, or break the tablets. If you have difficulty swallowing the 100 mg tablets, ask your healthcare provider for other VENCLEXTA options.
- Do not drink grapefruit juice, eat grapefruit, Seville oranges or marmalades, or starfruit while you are taking VENCLEXTA. These products may increase the amount of venetoclax in your blood.

When to stop taking VENCLEXTA

Do not stop taking this medicine unless your doctor tells you to.

If you forget to take VENCLEXTA

- If you miss a dose of VENCLEXTA by less than 8 hours, take the missed dose right away. Take your next dose the following day as usual.
- If you miss a dose of VENCLEXTA by more than 8 hours, do not take the dose that day. Take VENCLEXTA dose at your usual time the next day.

If you vomit after taking VENCLEXTA

- Do not take any additional dose that day.
- Take the next dose at the usual time the next day.

12. If you take too much

Talk to your doctor, pharmacist or nurse or go to hospital immediately.

13. How to store VENCLEXTA

Store at or below 30°C

14. What VENCLEXTA contains and what it looks like

Ingredients

- The active substance is venetoclax.
- Each film-coated tablet contains 10 mg, 50 mg or 100 mg venetoclax.
- The other ingredients are copovidone, polysorbate 80, colloidal silicon dioxide, anhydrous dibasic calcium phosphate, sodium stearyl fumarate.
- The film coating on all tablets contains: iron oxide yellow, polyvinyl alcohol, macrogol, talc, titanium dioxide.
- The 50 mg tablet film coating also contains: iron oxide red, iron oxide black.

Presentation

- VENCLEXTA 10 mg film-coated tablets are pale yellow, round 6 mm diameter, with V on one side and 10 on the other.
- VENCLEXTA 50 mg film-coated tablets are beige, oblong 14 mm long, with V on one side and 50 on the other.
- VENCLEXTA 100 mg film-coated tablets are pale yellow, oblong 17.2 mm long, with V on one side and 100 on the other.

Not all presentations may be available locally.

Manufactured by:
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