

Generic Name: **Venetoclax**Brand Name: **Venclexta**

Drug Classification: B-Cell Lymphoma-2 (BCL-2) Inhibitor

INDICATIONS FOR USE

- Venetoclax may be taken alone or in combination with another medication as an initial (first-line) treatment. When used as a combination therapy for front-line treatment, it is usually combined with obinutuzumab.
- Venetoclax can be given alone or in combination with rituximab as a second- or third-line therapy.
- Retreatment with venetoclax combined with obinutuzumab as a second- or third-line therapy can be prescribed 'off-label' by healthcare providers at their discretion. However, it is important to note that insurance plans may not cover the cost of medications that are prescribed off-label.

ADMINISTRATION ROUTE

Taken orally by mouth (in tablet, film coated form).

LENGTH OF TIME ADMINISTERED

- When Venetoclax is given in combination with another medication it is usually taken for a pre-determined, limited amount of time and then stopped (also called limited-duration, fixed-duration, or time-limited therapy). When venetoclax is taken alone (which is not common), it may be taken continuously until the CLL or SLL progresses.
- If you have previously untreated CLL or SLL then venetoclax is usually taken in combination with obinutuzumab for 12 months.
- If you have previously received treatment for CLL or SLL, then venetoclax is usually taken in combination with rituximab for up to 24 months.

DOSING

- Your healthcare provider will increase the daily dose amount each week for 5 weeks (this is called the ramp-up phase).
- The starting dose is 20 milligrams taken once per day.
- The maximum dosage does not exceed 400 mg per day.

MISSED DOSE

If a dose is missed by more than eight hours, it should be skipped. Then take the next dose at the regularly scheduled time. Do not take an extra dose to make up for the missed dose.

HOW TO TAKE THIS MEDICATION

- Take it with a meal and plenty of water.
- Do not chew, crush, or break tablets.
- Do not ingest any starfruit, grapefruit juice, grapefruit, bitter orange/marmalade products, or Seville oranges (these are known to interfere with the metabolism of

the medication and can potentially cause toxic levels of the drug to build up in the blood).

COMBINATION THERAPIES

Can be used in combination with other medications (such as obinutuzumab or rituximab) and/or various combinations of medications being studied in clinical trials.

COMMON SIDE EFFECTS

Side effects can occur as a result of any medication, some of which may go away with time as your body adjusts to the new medication. Please notify your healthcare provider right away if any of the following side effects occur:

- Low white blood cell count, low red blood cell count, and low platelet count
- Diarrhea, nausea, constipation, or vomiting
- Infection (upper respiratory, pneumonia, blood, or other infections)
- Cough
- Muscle, joint, stomach, mouth/throat, or back pain
- Decreased appetite
- Bloating or gassiness
- Swelling of the arms, legs, hands, or feet
- Fatigue or tiredness
- Tumor Lysis Syndrome (see special considerations below)

Other side effects not mentioned above may also occur. Notify your healthcare provider of any other unusual symptoms, as they may be able to tell you about ways to prevent or reduce certain side effects.

MANAGING COMMON SIDE EFFECTS

Some side effects are more common than others, many of which will go away after a short period of time after staying on the medication. It is important to talk to your healthcare provider to discuss if you might be able to manage side effects in the short term to stay on the therapy until your body has time to adjust to the new medication. Here are some possible ways to help manage some of the most common side effects of venetoclax in consultation with your healthcare provider.

Tumor Lysis Syndrome (TLS)

- You can help prevent TLS by staying well hydrated and drinking at least 60 ounces of water every day during the ramp-up phase, especially the first day of each dose increase. It is important to begin hydrating at least two days before the first dose begins.
- Your health care provider may recommend a medication called allopurinol to prevent the buildup of something called uric acid in the blood.

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- You will have frequent blood tests during the ramp-up phase so your healthcare provider can closely monitor for TLS.

Diarrhea

- Increase your fluid intake.
- Take anti-diarrheal medications (such as Imodium) per package instructions.
- Eat a bland diet (such as bananas, rice, apples/applesauce, toast, or plain pasta).

Constipation

- Increase your fluid intake.
- Consume more foods that are high in fiber (such as vegetables and whole grain bread).
- Consider over-the-counter fiber supplements (such as Fibercon, Miralax, or Metamucil).
- Move around more, as walking and other forms of exercise can help.
- Take over the counter stool softeners (such as Colace) to help soften bowel movements.

Fatigue or Tiredness

- Ensure you are eating a well-rounded diet that includes a balance of lean meats, fruits, vegetables, whole grains, and limited amounts of processed foods.
- Incorporate light types of exercise (such as walking).
- If you are able, take one short twenty-minute nap during the day. Frequent or longer naps during the day can affect the amount of sleep you are getting during the night and increase fatigue/tiredness.

Muscle, Joint, or Bone Pain

- Take acetaminophen (i.e., Tylenol) per package instructions.
- It is important to avoid taking anti-inflammatories (such as ibuprofen) for mild pain while taking venetoclax due to the slightly increased risk of bleeding.
- Antihistamines may help with bone pain.
- Magnesium supplements may help muscle cramping.
- Gentle stretching, application of heat or ice to affected area(s).
- Your healthcare provider may prescribe a short course of steroids for severe joint pain.

Nausea, Vomiting, or Decreased Appetite

- Eat small, frequent meals throughout the day instead of three large meals.
- Eat a bland diet (such as bananas, rice, apples/applesauce, toast, or plain pasta).
- Avoid acidic and spicy foods.
- Take anti-nausea medications as directed thirty minutes before you attempt to eat or take other medications.

Swelling

- Elevate your legs above the level of your heart when at rest.
- Try to move around and have as much light activity as possible.
- Limit the amount of salt intake in your diet.
- Wear compression stockings (if they are not contraindicated due to another medical condition).

REASONS TO TALK TO YOUR HEALTHCARE PROVIDER

The presence of other medical problems may affect the use of venetoclax. Make sure you tell your healthcare provider if you have any of the following conditions:

- High uric acid levels in the blood
- Kidney disease (you may still use with caution and close monitoring, but taking this medication may worsen the condition)
- Liver disease
- Gout
- Infection (this medication may decrease your body's ability to fight an infection)
- Pregnant or breastfeeding (or if you plan to become pregnant/breastfeed)

Always tell your healthcare provider about all the medications you take, including prescription and over the counter medicines, vitamins, and herbal supplements

SPECIAL CONSIDERATIONS

- Several medications can interfere with the metabolism of venetoclax and cause toxic levels to build up in the blood. It is important to provide a complete and thorough list of all the medications you are taking to your healthcare provider.
- A rare and potentially life-threatening event called tumor lysis syndrome (TLS) can occur upon treatment initiation, during the ramp-up phase, or during any re-initiation of venetoclax after a dosage interruption. TLS occurs due to the rapid killing of cancer cells, which happens so quickly that the body does not have time to clear out all the debris released from inside the cancer cells when they break open. This rapid uncontrolled release of the cell contents can potentially cause heart, kidney, and nervous system dysfunction. Your healthcare provider will assess your risk for TLS prior to initiating venetoclax. With close monitoring and preventative therapy, the likelihood of TLS can be greatly reduced.